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Public Health

GEAR, H. S. **The Medical Resources of the World Health Organization.** Reprinted from *Canadian Med. Ass. J.* 1958, May 1, v. 78, 704–8.

We have become accustomed to the idea of the World Health Organization, but we forget, or we may never have known exactly, its composition and scope, and it is useful to be reminded from time to time of the duties imposed on that body, and how they are discharged. Dr. Gear has held high executive office in WHO for a long time, and writes with authority; he also writes clearly.

The basic concept of WHO is to strengthen national administrations by providing advisory services to governments individually (482 projects in 127 countries in 1956), and by providing technical services on behalf of all countries, for instance by publishing epidemiological data, classification of disease, biological standards, etc.

It has 7 offices—headquarters and 6 regional offices—and at the end of 1956 employed 176 medical and related scientists and practitioners. The author discusses the organization of the regular staff, the consultants, the fellowship system, the advisory committees, the local medical institutions and their relation with WHO, the non-governmental associations, and the financial resources of WHO. He ends on a note of pride:—

"This world-wide system of arrangements by which so much of the world's medical resources are used is complicated. It has certain weaknesses. Its efficiency is not uniform. Many of its methods are still experimental. Nevertheless, in a relatively short time it has become a partnership of independent trained minds and institutions in a service co-ordinated and supervised by WHO by which the world is given the best of medical knowledge and guidance." *Charles Wilcocks*

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. No. 158. **Expert Committee on Medical Rehabilitation. First Report.** Geneva, 24–28 February 1958. 52 pp. [Refs. in footnotes.] 1958. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr.2.–.]

At its first session the Expert Committee on Medical Rehabilitation was requested, in an address by the Director-General of the World Health Organization "to consider the concept and principles of rehabilitation from the medical viewpoint" as well as "the aims of and methods for the planning of the organization and setting-up of the services it should include, taking into account the social and economic conditions peculiar to the different countries".

Because of the vastness of the field to be covered in rehabilitation the committee at this first session confined itself to "discussing general principles and practices of basic importance rather than details which could be dealt with in future sessions".

This first report of the Committee is of great interest and value. It is in 9 sections which cover:—(1) concept of medical rehabilitation in relation to social and preventive medicine, (2) its value, (3) the magnitude of the problem, (4) basic principles and aims, (5) the needs of the handicapped, (6) education and training of medical and allied personnel, (7) education of the public, (8) planning and organization of services and (9) recommendations for further study and action. These recommendations refer to the needs for precise definition of terms used in the rehabilitation concept, better statistical studies, greater cooperation between interested agencies in some instances and for developing better rehabilitation techniques for those disabled from circulatory, respiratory and digestive disorders.

There are 4 annexes to the report and the subjects of these are psychological aspects of rehabilitation (Annex 2), rehabilitation in the less developed countries (Annex 3), list of supporting documents (Annex 4) and selected data on the prevalence of physical impairments in some population groups (Annex 1). The numerical tables in Annex 1 set out some particulars from Canada, France and Great Britain by age, sex and population rates. In Great Britain the total number of disabled persons of both sexes registered in 1954 under the Disabled Persons (Employment) Act, 1944, was 839,210. *M. E. Delafield*

NORTHERN IRELAND, GOVERNMENT OF. **Report on Health and Local Government Administration in Northern Ireland during the Year ended 31st December, 1957.** Cmd. 387. pp. ix + 112, 5 graphs & 2 maps. 1958. Belfast: H.M. Stationery Office. [6s.]

This report is on similar lines to that of the previous year [this *Bulletin*, 1958, v. 33, 89].

The introduction by the Chief Medical Officer, Dr. Frank F. MAIN, indicates satisfaction with the position on tuberculosis (death rate 13 per 100,000), infant mortality (29 per 1,000 live births), diphtheria (deaths 0, cases 2) and whooping cough (deaths 2, cases 304) but unsatisfactory features were diarrhoea and enteritis in children under 2 (deaths 33 compared with 18 in 1956) and maternal mortality (1·1 per 1,000 live births compared with 0·56 in the previous year). The last was mostly due to deaths from toxaemia.

There was a sharp outbreak of poliomyelitis of virus Type 1 with 9 deaths and 225 notified paralytic cases mostly in the City of Belfast. In Northern Ireland as a whole 21,527 children under 10 received one or more injections of poliomyelitis vaccine. There was an extensive but mild epidemic of "Asian 'flu".

A comparative study has been made of the claims for sick pay in Scotland and Northern Ireland from which it emerges that in the latter there are fewer new claims for sickness benefit but the duration of illness is longer and there is more long-term illness.

The population of the province is 1,398,500 of whom 440,000 live in Belfast. The birth rate was 21·5 and death rate 10·9. The cancer death rate at 165 per 100,000 population is the highest yet recorded.

For all the principal statistics comparable figures are given for England and Wales, Scotland and the Irish Republic.

Apart from the introduction the rest of the volume deals with different aspects of the National Health Service, the local authority health and welfare services, housing and local government.

A separate report is published by the Tuberculosis Authority [this *Bulletin,* 1959, v. 34, 425].

The expenditure of the Hospital Authority for 1956–7 was £9,750,906, of which £1,857,540 was for capital as distinct from revenue purposes. The beds controlled by the Authority now number 15,578, of which 8,798 are in general and 6,313 in mental hospitals. There are employed in the hospitals 284 consultants and specialists, 408 other doctors and dentists and 5,772 nurses.

Over 6 pages are devoted to mental health, including a section on "special care" cases which is the Northern Ireland term for the mentally defective. Publicity for the purpose of removing public misunderstanding about mental illness and mental hospitals is active and is described.

There is a separate board for the General Health services which comprise the general medical, dental, pharmaceutical and supplementary eye services. There are 746 general medical practitioners on the medical list and the number of persons on the total of their individual lists exceeds slightly the total population of the province.

The ambulance service, for which the demand continues to grow, is administered by the Hospital Authority.

The net average cost per patient for drugs was £1 10s. 0·74d., which is ½d. more than in 1956.

Institutional confinement is gaining in popularity. Births in hospital were 17,999 and at home 11,850.

The work of local authority clinics is "expanding rapidly". A short section gives the salient findings of the school health service.

There is a scheme by which "special diets" are provided for those of all ages in need of them. The question of a combined service of home nurses, midwives and health visitors is discussed and is commended only in sparsely populated areas.

Of the 134 adulterated food samples, out of the 4,274 examined, 75 were of minced meat or sausages.

During the year 6,500 new houses were completed.

[This is a comprehensive report of an active department which sets out impartially its achievements, its weaknesses and where further development is needed.]

Allen Daley

CHARRON, K. C. **Public Health and the Hospital Insurance and Diagnostic Services Program.** *Canadian J. Pub. Health.* 1958, Aug., v. 49, No. 8, 323–34, 2 figs.

Canada is feeling its way with regard to the problems of medical care. The Federal government has for some time made "health" grants to the provinces and these can be used to help with technical advisory services (standards), research and training as required for health insurance purposes. The Federal government now proposes to give financial aid towards provincial insurance schemes for hospital treatment and diagnosis. It is primarily for in-patient care but a Province may opt to include out-patient services in its scheme. Participating Provinces must ensure that "adequate standards are maintained in hospitals". In small hospitals the requirements may be quite simple. Provision can be made for some of the more specialized services such as laboratory, radiological or other diagnostic procedures, and a consultant to interpret them to be on a regional or even provincial basis. The drugs which can be provided as part of the insured service will be listed after consultation with the medical profession. A rehabilitation service can be included in the provincial scheme.

The greater part of the paper is devoted to the public health implications of this new Federal insurance programme. The need for coordination and integration with the other health services at all levels is emphasized.

Though there are at Federal level separate divisions, each with a Principal Medical Officer, for "Health Grants" and "Health Insurance", they are both within the department of the Director of Health Services and a joint administrative section has been set up to coordinate their activities.

The Provinces must designate a provincial authority for administrative purposes and this may be (a) the health department, (b) a commission reporting to the provincial legislature through a responsible minister, (c) a commissioner in the provincial Ministry of Health and of deputy minister status, or (d) a named commissioner largely concerned with insurance matters and responsible to the minister of health but with the health department having responsibility for hospital standards.

Whatever the arrangement, the common areas of interest between the health departments and the local hospital insurance and diagnostic services programme

include child and maternal health, nutrition, epidemiology, laboratory services, medical rehabilitation, home care and health units.

Close relationship between the two sides is essential. The provision of morbidity statistics by the hospitals should be an aim. *Allen Daley*

Maternal and Child Health

BULL. MÉD. DE L'A. O. F. 1958, v. 3, Special No., 98 pp., 3 figs. on 3 pls., 1 diagram & 1 plan. Les Journées médico-sociales de Dakar, 28–29–30 Octobre 1957 [**Medico-Social Conference, Dakar, October 1957**].

A 3-day medico-social meeting at Dakar was devoted to discussions on maternity and child welfare and alcoholism in French Africa. The foundation stone of a rural centre for family protection was laid. This is to follow the pattern of an established centre at Soissons, in metropolitan France, at which educational activities of all kinds related to infant and child welfare are undertaken, and which is attended by workers from many lands. In Africa, where rapid economic development and infant mortality rates of 400 or more per 1,000 live births exist side by side, there is obvious need for such a preventive medicine institution. The young doctor new to the bush, and the rural nurse and midwife, will receive practical instruction, and courses for international students are planned.

Speakers were agreed that after the major epidemic and endemic diseases have been brought under control, maternity and child welfare is one of the most important aspects of the consolidation of public health. There should be centres in every locality, which could combine curative and preventive procedures, with due precautions against cross-infection. Such centres exist already in several large towns. In rural areas, regular visiting clinics take the place of static centres. The instruction of traditional midwives in hygiene was recommended. There were divergent opinions on the prevalence of congenital syphilis, but all were agreed that the condition does occur throughout French Africa, and that the provision of facilities for serological testing at ante-natal clinics is a matter of urgency. A more active school health programme was suggested, a feature of which would be the participation by senior scholars in medical, nutritional and sanitation procedures, in the school and neighbouring district. The need to expand the social services was stressed: apart from the multitude of tasks performed by trained social workers, local girls thus trained eventually take their place in the community as mothers and disseminate enlightened social and hygienic standards. Médecin Général RICHET spoke on the contribution to maternity and child welfare made by the work of the SGHMP [see LE ROUZIC & KOCH, *Trop. Dis. Bull.*, 1950, v. 47, 444] itinerant medicine designed in terms of mass cure and prevention of endemic disease, reaching everyone even in the most remote rural areas, and maintaining the closest possible liaison with static medical services. Campaigns against smallpox, yellow fever, epidemic diseases, trypanosomiasis, treponematoses and leprosy all benefit mothers and children. Malaria, tuberculosis, trachoma and onchocerciasis are being tackled in increasingly large areas. [The present policy of the SGHMP is well set out in this brief paper. It is particularly interesting to note that the mobile service is staffing an increasing number of static rural treatment centres, a natural development of field medical services which is taking place in other territories too.] Professor J. SÉNÉCAL spoke on training, stressing the fact that training on the problems of Africa should be conducted in Africa. Courses on paediatrics are held in association with the medical school at Dakar. He suggested the creation of a class of medico-social *aides*, to receive a year's medical training and a second year's in-service training with medical and social workers.

In the session on alcoholism, there was some divergence of opinion, unsupported by statistics on either side, as to the extent of serious alcoholism in French Africa. All were agreed on the desirability of limiting imports of alcoholic drinks, and of organizing temperance propaganda. *B. B. Waddy*

PHILIP-WERTHEIMER, Janine. La protection maternelle et infantile à Cayenne. [**Maternal and Child Welfare in Cayenne**] *Bull. Acad. Nat. Méd.* 1958, v. 142, Nos. 29/30, 782–8.

In Cayenne a maternal and child welfare service was started in 1950 for the population of some 17,000 out of the total population of French Guiana of 30,000. In 1957 a proper dispensary building was opened and by the end of the year 1,500 pregnant women and 2,923 children were being looked after. Some 55% of the children proved to be born out of wedlock. Interesting ante-natal findings concern syphilis (11% positive in 1957), tuberculosis (only one case found in 1,012 examined) and leprosy, which has a general incidence of 5%. The increase in weight of mothers during pregnancy was only 3 kgm. instead of an expected 10 kgm., probably because of low standards of living and diet, but the infant at birth was of normal weight. A significant number of the mothers were aged 13 to 15 years.

At the children's clinics some 500 new babies were seen annually. Infant deaths amounted to between 26 and 43 yearly in some 650 live births but only 2 died of the children supervised in the clinic in each of the last 2 years. A free gift of cereal food is given when the child is aged 4 months and the mother is shown how to prepare it; calcium is given at the 6th month if the teeth have not appeared. Between the 2nd and 6th years children are seen 4 times yearly and are

dewormed with chenopodium each time. In addition the mothers are asked to assist by giving a piperazine vermifuge monthly because this improved the child's general condition. Protein deficiency is a problem but communicable diseases are not. Owing to resistance by mothers, smallpox vaccination is deferred until admission to infant school at 2 to 3 years of age. BCG is given to all school-children. This small service is clearly being successful as is shown by the infant mortality which has fallen from 65 per 1,000 in 1955 to 40 per 1,000 in 1957. *T. H. Davey*

MEDICAL J. MALAYA. 1958, Sept., v. 13, No. 1, 1–122, 4 figs. [Numerous refs.] **A Five Year Survey of Obstetrics in Selangor.**

This issue of the journal is almost completely taken up by a series of papers by D. LLEWELLYN-JONES. He writes on heart disease and toxaemias of pregnancy, eclampsia, haemorrhage, placenta praevia, prolonged labour, malpositions, multiple pregnancy, difficulties of labour, induction of labour, caesarian section, forceps deliveries, puerperal pyrexia, maternal deaths and premature babies.

In addition there is a paper by P. W. G. TASKER on anaemia in pregnancy, and one by R. S. MCCOY on perinatal mortality.

The whole series relates to conditions as they are seen in Malaya, and the papers are based on original observations made over the period 1953 to 1957; the reports follow the pattern recommended by the Royal College of Obstetricians and Gynaecologists. This collection of first-hand information is obviously valuable for practitioners and future students.

Charles Wilcocks

FOLL, C. V. **The Perils of Childhood in Upper Burma.** *J. Trop. Pediatrics.* London. 1958, Dec., v. 4, No. 3, 122–6.

A questionnaire concerning their maternity histories and the fate of their children was answered by 1,107 wives of employees in an oil company in Chauk, Upper Burma. This paper records the findings, and also the findings on patients admitted to paediatric wards, and comments on the need for better hygiene and better ante-natal and paediatric care. There were only 15 nulliparae and each parous woman had on average produced 4·39 live children. There were 105 stillbirths in 4,794 deliveries. The stillbirth rate was 21·1 per 1,000 but for mothers aged 15 to 25 the rate was 44·3, probably because primiparae return home for the first delivery and are exposed to vigorous massage and intramuscular pitocin. Neonatal mortality was 40·1 per 1,000 live births compared with 57·1 for 37 towns in Burma. This high rate was probably due to bad midwifery and low birth weight; the average birth weight was 6 lb. 7 oz. for boys and 6 lb. 3 oz. for girls, with 28% of boys and 26% of girls under 5½ lb. at birth. The total infant mortality was 163·4 per 1,000 live births, as compared with an average of 248 for the years 1947–56 in Burma. The causes of infant mortality were inadequate breast feeding, often only 10 to 12 oz. daily, and fly-borne intestinal infections. The mortality during the first 5 years was 217·1 per 1,000, mainly caused by bowel infections, dysenteries and respiratory infections. Tuberculosis is common, usually as cervical adenitis or tabes mesenterica, probably of human origin. Enteric fever is common but deficiency diseases are not. *T. H. Davey*

TAYLOR, Dorothy M. & GORRIE, Mary G. **The Integration of Health Services for Children.** *Pub. Health.* 1959, Jan., v. 73, No. 4, 123–9.

In this paper the authors review the present position of the health services for children provided under the National Health Service Act and "consider what requires to be done, to improve and develop the existing services, for the care of children in sickness and health". Particular attention is paid to the position, function and training of those medical personnel who serve the child in various capacities, *viz.*, general practitioners, paediatricians, "specialist" consultants, assistant medical officers for maternity and child welfare, school medical officers and medical officers of health. The work carried out by these is shortly described with comments and the lines of future policy are discussed. Future developments are discussed with suggestions on "how the different medical groups might operate separately, and collectively, to form a child health team", with indications of "ways in which the general practitioners might be encouraged to play a more important part in the preventive services, and how the assistant medical officers for child welfare, and school health, can be made to feel responsible members of the health team". Some ideas are also offered on "how the medical officer of health, and the senior maternity and child welfare officer, can influence the integration of the existing services in their area, not only by their own efforts and those of their staffs, but also by co-operation with general practitioners and paediatric colleagues". *M. E. Delafield*

ACHESON, R. M. **The Environment and the Growth of Children.** *Irish J. Med. Sci.* 1959, Jan., 6th Ser., No. 397, 11–19, 7 figs. [14 refs.] Discussion 20–22.

This paper is a short review of the work done by the author, who is the author or joint author of the 14 papers in the bibliography. Sickness and temporary adverse environmental circumstances have the effect of slowing growth. In Irish institutional children it was found that the girls had a retarded rate of growth for the first 9 months after admission and then despite the same diet and care their growth accelerated during the fourth quarter of their stay. Girls in these institutions also showed a falling off in the rate of growth after a severe fever. When growth has been interrupted it is not certain whether this is compensated for later or whether there is some permanent stunting. The result of strain on the growth pattern appears to differ between the sexes. It would seem that in addition to the genetic pattern, environment is an important factor affecting growth. *W. J. Martin*

DAWSON, Jean P., THAYER, W. W. & DESFORGES, Jane F. **Acute Hemolytic Anemia in the Newborn Infant due to Naphthalene Poisoning: Report of Two Cases with Investigations into the Mechanism of the Disease.** *Blood.* 1958, Dec., v. 13, No. 12, 1113–25, 4 figs. [58 refs.]

At least 18 cases of acute haemolytic anaemia after exposure to naphthalene have been reported since 1949. In this paper there is a description of 2 cases of this condition in new-born children with a report on the investigations of erythrocyte metabolism in these infants and their families.

The cases occurred in Negro infants, a 14-day-old female and a 9-day-old male who were admitted to the Boston City Hospital because of icterus and pallor. Both infants were normal at their birth in hospital and only became ill after returning home, where the girl was dressed in "clothing heavily impregnated with naphthol" and the boy in "clothing impregnated with naphthalene mothballs". Both children recovered. Their states on admission are described with details of the results of blood examinations.

The biochemical investigations of the peripheral blood of the 2 patients and some of the members of their families which were carried out are described in detail. These studies included examination of Heinz bodies, glutathione determination, glutathione stability, methaemoglobin reduction, glucose-6-phosphate dehydrogenase activity and glutathione reductase. The findings of these studies are described with tables and figures and there is a long discussion and many references.

In both infants there was "glutathione instability upon incubation with acetyl phenyl-hydrazine and naphthol months to years later. Several members of their families exhibited a similar defect with evidence that it is inherited as a simple dominant". In those individuals with glutathione instability there were indications of deficiency in glucose-6-dehydrogenase activity.

M. E. Delafield

VAN BENTHEM, L. H. B. M. & VAN ZAANE, D. J. Cerebellaire verschijnselen bij thalliumvergiftiging. **[Cerebellar Symptoms of Thallium Poisoning]** *Nederl. Tijdschr. v. Geneesk.* 1959, Jan. 24, v. 103, No. 4, 148–52. [15 refs.] English summary (8 lines).

3 children admitted to the neurosurgical centre at Tilburg (Holland) with the diagnosis of a cerebellar condition were found eventually to be suffering from thallium poisoning. In each case subsequent investigation showed that they might have been in contact with a thallium salt used to kill rats and mice.

The authors give a detailed description of the clinical picture. 1 patient was even operated on for a cerebellar tumour. 1 patient died.

The authors complain that thallium salts are much too easily obtained and in any case are now quite unnecessary as rodenticides. *W. K. Dunscombe*

DOUGLAS, J. W. B. & BLOMFIELD, J. M. **Children under Five.**

This book is reviewed on p. 511.

Vital Statistics and Epidemiology

SIGNORINI, L. F. & GATTA, A. M. La mortalità infantile a Firenze tra il 1945 e il 1956. **[Infant mortality in Florence from 1945 to 1956]** *Ann. d. San. Pubblica.* Rome. 1958, Sept.–Oct., v. 19, No. 5, 987–1017, 8 figs. [21 refs.] English summary.

In the 12 years 1945–56 there were in Florence 2,089 deaths under the age of 1 year. The authors have studied them in detail, for each calendar year separately and in relation to sex, legitimacy and certified cause of death. The infant mortality rate was very high in the immediate post-war years (70–80 per 1,000) but it has fallen steeply to only 27 per 1,000 at the end of the period. The decline has been particularly striking in the illegitimate babies so that in the final 3 years their rate of mortality (about 36 per 1,000) has not been greatly above that of the legitimate (26 per 1,000). The main causes of death contributing to this general betterment have been those attributed to immaturity, bronchopneumonia and gastro-enteritis. In the final 7 years deaths from gastro-enteritis have been conspicuously few. Birth injuries and congenital malformations, on the other hand, have shown no improvement. In the 12 years as a whole nearly 70% of the deaths took place in the first month of life. *A. Bradford Hill*

BÉHAR, M., ASCOLI, W. & SCRIMSHAW, N. S. **An Investigation into the Causes of Death in Children in Four Rural Communities in Guatemala.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 6, 1093–102, 1 fig. [Refs. in footnotes.]

The death rate in Guatemala is very high, the crude death rate in 1953 was 23·2 per 1,000, the infant mortality in 1955 was 101·4 and the death rate at ages 1–4 years was 42·1 per 1,000. For the country as a whole only one death in every 8 was medically certified, the remainder were classified by the town registrar's interpretation of the information obtained from the relatives. The experience of health workers suggested that infectious diarrhoea and malnutrition, particularly kwashiorkor, were important causes of death although official statistics did not reflect their importance as a cause of death among children.

The present paper was based on 353 deaths, of which

222 were of children under 15, and none of which was medically certified, in 4 highland villages during 1956 and 1957. These villages had a somewhat higher infant mortality (136·8) and death rate at ages 1–4 (50·3) than the whole country. The method adopted was for a trained worker to visit the family where a child aged under 15 years had died, to complete a questionnaire from information obtained from the parents or other observers and if possible to view the body. On the basis of this information the cause of death was classified and a comparison was made with the causes in the official statistics. The most striking discrepancies were those of intestinal parasites to which 58 deaths were assigned by the official statistics and none by the field enquiry, and kwashiorkor to which 40 deaths were ascribed by the field enquiry and none by official statistics. This difference arose from the local belief that the signs and symptoms of kwashiorkor are caused by worms and this belief is strengthened by the frequent finding of *Ascaris* in the stools of children with diarrhoea. No deaths occurred from kwashiorkor under one year of age.

Deaths from diseases of the digestive system were at a maximum during April to August and deaths from kwashiorkor from May to October. Whether kwashiorkor was a primary or contributory cause of death is a matter of doubt. The authors suggest that cases of kwashiorkor would not develop without the precipitating strain of diarrhoeal or other infectious diseases. They conclude that the nutrition of the young child must receive more attention in their public health programme if the death rates are to be reduced.

W. J. Martin

MINISTÈRE DE LA SANTÉ PUBLIQUE. Paris. Pathologie régionale de la France. Vol. II. Régions du Nord, de l'Est et du Centre [Ministry of Public Health, Paris. **Regional Pathology of France. Vol. II. North, East and Central Regions**] [MAROT, R.]. *Monographie de l'Institut National d'Hygiène No. 17.* 419 pp., numerous figs. [Numerous refs.] 1958. Paris (16e): Inst. Nat. Hyg., 3, rue Léon-Bonnat. [3,400 fr.]

The data in this volume, which covers the central, east and north regions of France, are displayed in the same manner as in the first volume, which dealt with the southern and western regions of the country [this *Bulletin*, 1959, v. 34, 10]. The epidemiological study of each region is preceded by a description of the geographical, climatic and socio-economic characteristics of the area. The epidemiology of the infectious, contagious and parasitic diseases is given in detail but for most of the diseases the presentation is descriptive and little statistical information is given. A list of references is, generally, given at the end of the discussion of the various types of infective diseases. Under the heading of the great social scourges the author lists (A) tuberculosis, (B) venereal diseases, (C) cancer, (D) alcoholism, (E) rickets, endemic goitre, infant mortality and mental illness. The mortality from tuberculosis has fallen considerably in recent years and in the departments of the central region the mortality in 1955 varied from 23 to 59% of that in 1949, in the departments of the eastern region from 29 to 58% and in the departments of the north-east from 44 to 59%. The actual death rate ranges from 23 to 40·6 per 100,000 in the departments of the 3 regions. The statistics given for venereal diseases all relate to the pre-war period. The crude death rate from cancer has risen during the past 20 years and in 1948–55 the death rate per 100,000 population ranged from 145 in Haute-Saône to 226 in Haut-Rhin. The sales of alcohol have been analysed in detail but the data relate to the pre-war years. It would appear from the tables that the inhabitants of the north of France were the greatest consumers of alcohol. Alcoholism due to wine affects the central nervous system while excessive beer drinking gives rise to digestive and stomach disorders.

Paris and the surrounding country has been dealt with at length (173 pages). The problems of food and water supply, sewerage, travelling, housing, migration in Paris are discussed briefly. The effects of food rationing during the war years are briefly reviewed.

There are differences in the pattern of disease between regions and between departments in the same region but the lack of statistics prevent a concise comparison being made. Climatic and geographical position account for some of the differences between areas and certain districts have their own peculiar hazards. Malaria is endemic in the plain of Forez with its large number of ponds and swamps. The risk of avalanches, the effect of living in high altitudes, skiing accidents (the type of accident and nature of injury are described in detail) is confined to mountainous areas. The miners of Saint Etienne are at risk of ankylostomiasis since the warm humid working conditions are ideal for the existence of the parasite. The influence of social economic factors in the life of the population is, perhaps, most marked in the industrial towns of the north and between the various *quartiers* of Paris.

A list of watering places is given in each section of the book together with the situation of the spas and the chemical constitution of the water. *W. J. Martin*

PACY, H. **Morbidity Recording in a Small Country Practice.** *Med. J. Australia.* 1958, Nov. 22, v. 2, No. 21, 693–6, 4 figs.

Records have been maintained for 3 years (1954–7) in a one-man practice of 980 persons in a New South Wales coastal district. An analysis of cases by aetiology (according to the International Classification of 1948) showed that 43% of the total were due to non-specific inflammation and infections, 20% to trauma, 9% to psychic or psychosomatic illnesses and 8% to degenerative disease. Under analysis by morphology the skin and underlying tissues occupied first place (26%) owing partly to the large number of occupational accidents in the local timber trade. It was followed by the respiratory system (17%) and cardio-vascular system (10%). Classification by specialties remits 42% of the conditions to the physician, 20% to the surgeon, 13% to the dermatologist and 9% to the gynaecologist or obstetrician. Using these illustrative data the author makes a plea for a comprehensive system of continuous morbidity recording to cover the diagnostic,

therapeutic and economic aspects of illness. He suggests a 5-yearly assessment of such records by the Registrar-General. *A. Bradford Hill*

BRITISH J. CLIN. PRACTICE. 1958, Nov., v. 12, No. 11, 751–840, numerous figs. [Numerous refs.] **Symposium on Tuberculosis** [HEAF, F. (Edited by)].

In his ignorance the reviewer does not know the exact function and status of a Guest Editor. Professor Heaf is stated to occupy this position in a symposium on tuberculosis which occupies most of the November number in the *British Journal of Clinical Practice*.

In this collection of papers 9 are contributed by workers associated with the Welsh National School of Medicine at Cardiff, and 2 from Bristol and 1 from Oxford. It would appear from Professor Heaf's introduction that the symposium is compiled to give the general practitioner a concise account of the present position of tuberculosis, particularly in Great Britain. Those who know Professor Heaf will not find it difficult to find evidence of his skilful marshalling of the contributors. All important aspects of the subject are covered, the information is thoroughly up to date, and there is little of the overlapping which is frequently a source of irritation to readers of symposia.

It is, therefore, not surprising that W. Powell PHILLIPS, Medical Officer of Health for Cardiff, contributes the first article—on *Tuberculosis in Relation to Public Health* (p. 751). He shows clearly by graphs the enormous fall in the death rate of tuberculosis in England and Wales which has taken place recently, and the drop which more belatedly has occurred in the notification figures. He tries to correct the idea that the battle against tuberculosis is already won, and indicates the modern public health approach. This warning is of great importance as it has been encouraged by what many workers consider to be a premature change of title by the National Association for the Prevention of Tuberculosis. This also is very rightly emphasized in S. H. GRAHAM's paper on *Present-day Tuberculosis Problems of a Chest Clinic* (p. 757). There is a considerable danger that in the modern chest clinic the all-important work of prevention of infectious disease will take a back seat to the exciting clinical problems of non-tuberculous chest disease.

These papers lead to a more didactic account of *Tuberculin Testing and B.C.G. Vaccination* (p. 791) by K. Neville IRVINE. He advocates the use of the Heaf multiple puncture test for routine work, and all recent evidence supports this view. Resistance to this test by children and parents is much less than to the Mantoux test and the saving of skilled medical manpower is considerable when compared with the Mantoux method. Now that the efficiency of the freeze-dried BCG is accepted he advocates that much of this immunization should be done by general practitioners. This idea will not meet with universal acceptance.

A very clear and competent account of the radiological problems is given by J. H. MIDDLEMISS from the United Bristol Hospitals—*Present Radiological Problems in Relation to Respiratory Tuberculosis* (p. 822). By inference he suggests that the present tendency in the interpretation of chest films solely by chest clinicians will give inferior results to those given by a radiologist and chest physician working in unison. The reviewer having had the advantage of this team work in his hospital clinics would agree, provided that the radiologist is an expert in chest work; but whether the considerable amount of money required for salaries of radiologists if undue delay is to be avoided, could not be put to a better use is an arguable point; perhaps the man-power could be obtained if the unnecessary barium meals caused by fear of legal action could be avoided.

Another aspect of the radiological problem is dealt with in T. Francis JARMAN's article—*Tuberculosis in Industry—the Role of Mass Radiography* (p. 826). He describes the groups in which mass X-rays are most profitable, with special reference to trades where pneumoconiosis is common. His enthusiasm for mass radiography of industrial workers is hardly supported by the figures which he gives of the percentage of cases discovered compared with those found in other groups. J. MARKS, in describing *Advances in Tuberculosis Bacteriology* (p. 763), provides up-to-date material of chromogenic and atypical bacilli which he rightly calls indeterminate, and he adds some notes on the sensitivity problems.

In recent years the pathology of the various lesions found in pulmonary tuberculosis has become much clearer. R. M. E. SEAL describes these in a short, but very sound, article—*The Pathology of Pulmonary Tuberculosis* (p. 769), and describes their relationship. Though necessarily dogmatic, there are few conclusions which are not generally acceptable. For the purpose for which it is intended it must be highly commended.

Any article covering problems of pulmonary tuberculosis in children must overlap to some degree that on pathology generally. It is probably owing to the opinions held by Mr. Dillwyn THOMAS the surgeon —that surgery in children with pulmonary tuberculosis is often indicated—that J. JACOBS has received material which is not usually available to the paediatrician. In his *Concept of Pulmonary Tuberculosis in Childhood* (p. 778) he shows how he has taken advantage of such opportunities. This article appears to the reviewer to be outstanding in clarity of presentation on a subject which is full of obscurities to those who are not fully familiar with the subject. Some will not agree with the emphasis he places on surgery, for it must not be thought that the brilliant success and low mortality achieved at Sully can be readily obtained elsewhere. The author can be congratulated on an excellent paper.

The selection of A. T. M. ROBERTS and H. R. S. HARLEY to contribute the article on *The Chemotherapy of Tuberculosis* (p. 797) and *The Place of Surgery* (p. 803) was very happy; their ideas are mutually complementary, and as differences of opinion, however justifiable, are merely muddling in a symposium of this type, this is very advantageous. Combined, they give an excellent account of generally accepted practice in treatment. Dillwyn EVANS was faced with an unenviable task when he undertook to deal with *The Diagnosis and Treatment of Skeletal Tuberculosis* (p. 811) in 10 pages, less a good deal of space taken up by X-ray reproductions which form a feature of the format of the symposium. The process of eradication of bovine

tuberculosis has cut down radically the occurrence of this type of disease. Within the limitation of space he has contributed a sound and workmanlike article rightly emphasizing the importance of impairment of function as an indication of the presence of early disease, the diagnosis of which is so important if good functional results are to be obtained.

Whether the concluding article—*Tuberculosis in the Tropics* (pp. 834–40), by Professor Heaf—is strictly relevant to this symposium is open to question; but it would be a pity if the article were omitted as Professor Heaf is one of the world's experts on this problem. The article sets out clearly the conditions and problems occurring in tropical communities, and emphasizes the cruel dilemma which is present when the money available is so much short of the needs—shall it be spent on treating individuals or on public health measures? In the long run the latter is undoubtedly the most paying, but public opinion will not allow such a course to be carried out to its logical conclusion.

The symposium can be unreservedly commended to those for whom it is intended. Tuberculosis has tended to be segregated; many general consultants who have little contact with it have a very sketchy acquaintance with recent advances, and will find this symposium a short cut to remedy the gaps in their knowledge.

F. H. Young

Communicable Diseases

For the bacteriology of these diseases see the section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order: General; Diphtheria, Whooping Cough, Streptococcal Infections, Staphylococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis, Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Encephalitis; Enteric Fevers.

GRUMBACH, A. & KIKUTH, W. **The Infective Diseases of Man and their Causative Organisms.**

This book was reviewed on p. 404.

PETERSDORF, R. G., FORSYTH, B. R. & BERNANKE, D. **Staphylococcal Parotitis.** *New England J. of Med.* 1958, Dec. 25, v. 259, No. 26, 1250–54.

Between February and June 1958, 7 patients, all except 1 over 70 years old, developed staphylococcal parotitis: all the patients were severely ill from other causes. The onset of parotitis was not closely related to recent operations—3 patients had had no operation—but dehydration may have been a factor of importance and possibly tracheostomy, present in 2 patients. The staphylococci were, in general, resistant to penicillin, streptomycin, the tetracyclines, chloramphenicol and erythromycin but sensitive to neomycin, bacitracin, novobiocin and vancomycin. Sensitivity patterns did not correlate clearly with phage typing but 3 of 6 strains and 3 of 4 typable strains were lysed by phages 80 and 81, now recognized as indicating very virulent strains often responsible for hospital outbreaks. Treatment of the patient with antibiotics did not prevent the development of parotitis—indeed in 5 of the 7 patients, parotitis developed while antibiotics were being given or closely thereafter. *A. B. Christie*

DÓBIÁS, G., BALLÓ, T. & KEMÉNYVÁRI, J. II. Die Bedeutung des Staphylokokken-*alpha*-Antitoxintiters bei den Pyodermien von Säuglingen, Kindern und Erwachsenen. [**II. The Significance of the Staphylococcal α-Antitoxin Titre in Infants, Children and Adults suffering from Skin Infections**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, Nov.–Dec., v. 116, Nos. 5/6, 385–404, 10 figs. [21 refs.]

The titre of staphylococcal α-antitoxin was measured in the serum of children of various ages and found to be lowest (mean 0·35 unit per ml.) at the age of 1–3 months. This was the commonest age for children to present with pyodermia. When children with or without pyodermia were compared, however, the former tended to have the higher titres. A number of somewhat complex relations between titre, age and chronicity of disease are presented [without any indication of the numbers of cases on which the figures are based]; in general, acute solitary lesions in infants or young adults were often associated with higher titres than multiple lesions. Nevertheless the serum antitoxic titre is considered a good indication of the immunity of the body, though other factors than α-antitoxin must be involved. Antitoxic titres determined *in vivo* did not differ from *in vitro* measurements. *R. E. O. Williams*

VENCLÍK, H. & POTUZNÍK, V. Über die Anwendung von Plasma mit höherem Antitoxingehalt bei Staphylokokkeninfektion. [**Use of Plasma with a High Antitoxin Titre in Staphylococcal Infections**] *Ztschr. f. ärztl. Fortbildung.* 1958, Dec. 15, v. 52, No. 24, 1033–5.

As active immunization in patients with acute staphylococcal infection is unsuitable because of the slow development of antibodies, the authors of this

short paper decided to make use of staphylococcal antitoxins contained in the blood of blood donors for passive immunization because preparations of gamma globulin from hyperimmune antitoxic human or animal sera were not available.

In a preliminary study blood samples from 420 patients in an ear, nose and throat department and 500 blood donors were examined, by methods which are described, to determine the titres of antistaphylococcal α toxin. The results of this study are described with a discussion, and a table sets out the titres of antitoxin at different age-groups from 0–6 months to over 50 years. For the purpose of obtaining the supply of immune plasma for treatment the blood of every donor was tested for its antibody content and only those samples in which the titre of staphylococcal antitoxin was high were used for separating immune plasma. Transfusion of this plasma into patients suffering from various staphylococcal infections had excellent clinical results in that the general condition improved rapidly, the fever lessened and healing was hastened. It is considered also that the plasma may be used with benefit as a preventive of staphylococcal infection particularly in dystrophic infants and weakly children. *M. E. Delafield*

SILVERTHORNE, M. C. **Staphylococcal Bacteremia and Osteomyelitis successfully treated with Novobiocin.** *Arch. Intern. Med.* 1959, Jan., v. 103, No. 1, 133–9, 3 figs. [11 refs.]

"A case of disseminated staphylococcal infection is reported, in which novobiocin therapy was used effectively. The case presents several interesting features: (1) the dramatic response to the drug, including the arrest and apparent reversal of destructive bone lesions; (2) the marked in vitro bactericidal effect of the antibiotic, and (3) the appearance of adverse reactions to the drug, which cleared as the drug administration was continued, so that the patient was able to complete a 7-week course of novobiocin therapy."

BERNI, A. & STELLA, F. Contributo alla profilassi della scarlattina con penicillina in collettività infantili. **[Contribution to the Prophylaxis of Scarlet Fever with Penicillin in an Infant Community]** *Nuovi Ann. d'Igiene e Microbiol.* 1958, Nov.–Dec., v. 9, No. 6, 473–84. [27 refs.] English summary.

The authors review the incidence of and mortality from scarlet fever in Italy in the years 1947–57. They agree that the decrease in virulence of the disease has rendered any campaign of specific prophylaxis unnecessary as regards the disease in ordinary communities and families. Where young children are gathered together in communities there may be a definite case for such prophylaxis as ordinary methods of isolation and the like prove ineffective. With regard to institutions such as summer camps and colonies parents are apt to be alarmed when informed that their children have been hospitalized and the children themselves are deprived of the benefit of their stay in such colonies; moreover, in such uncontrolled outbreaks, severer types of the disease may occur.

The authors describe 2 outbreaks of infection in 2 summer camps in 1956 and in 1958. In the first, 27 cases of scarlet fever occurred within 11 days of the first case. One intramuscular injection of a penicillin preparation containing 300,000 units of potassium penicillin G, 300,000 units of procaine penicillin and 600,000 units of dibenzylethylene-diamino penicillin was then given to 191 children aged between 6 and 12 years: no further case of scarlet fever developed in a 20-day observation period. In the second episode, penicillin was given immediately after the first case and no further cases developed. The children experienced no inconvenience from the injections and there were no severe reactions. The possibilities of interfering with host immunity to the haemolytic streptococcus or of producing a penicillin resistant streptococcus are not regarded as serious at the moment, a finding with which most workers would agree. *A. B. Christie*

SCHULTZ, I. & FRANK, P. F. **The Prophylactic Use of Sulfamethoxypyridazine (Kynex) during a Streptococcal Epidemic.** *Amer. J. Med. Sci.* 1958, Dec., v. 236, No. 6, 779–85, 2 figs. [15 refs.]

In an American naval recruiting centre during the winter of 1957–8, certain men, who were excluded from benzathine penicillin prophylaxis against streptococcal infections and rheumatic fever because of penicillin or other allergy, were given 2 gm. or 3 gm. of sulphamethoxypyridazine (Kynex) once weekly for the same purpose. Among 154 men so treated only 10 acquired bacteriological infections with streptococci, compared with 27 among 171 controls—a significant difference. Side effects, drug fever, rash, nausea, vomiting and headache occurred in 7·1% of the Kynex-treated men, but were severe only in 2 cases. Although streptococci, once acquired, cannot be eradicated by sulphonamides, clinical infection and rheumatic fever may be prevented if adequate blood levels are maintained. It would seem from this experience that 2 or 3 gm. Kynex once weekly may be sufficient for this purpose but that side effects may be troublesome. *H. Stanley Banks*

RITCHKEN, J. **Erythema Infectiosum.** *Central African J. of Med.* 1958, Nov., v. 4, No. 11, 486–7.

This is a short article describing 4 cases of erythema infectiosum (fifth disease) occurring in 2 families. They were all typical cases, occurring in children 5–10 years old and exhibiting the violaceous maculo-erythematous rash, developing later a lace-like pattern and present mainly on the extensor aspects of the limbs. The interval between the 2 cases in each family was about 8 days. A short description of the disease culled from 3 standard textbooks is given.

H. Stanley Banks

MONNET, P., SOHIER, R. & FREYCON, F. Réaction cutanée d'allergie et réaction de fixation du complément au cours de deux épidémies d'oreillons. Recherches sur leur intérêt pratique. **[The Skin**

Reaction and the Complement-Fixation Test during the Course of 2 Epidemics of Mumps] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1958, June, v. 6, No. 4, 335–48. [21 refs.]

After the admission on separate occasions of 2 children suffering from unrecognized mumps meningo-encephalitis 2 secondary cases of mumps occurred among 30 boys and 20 girls in the 2 paediatric wards concerned, and the authors have carried out an investigation of the subsequent development of immunity to mumps by means of skin tests with allantoic fluid antigen and complement-fixation tests. The results of the investigations are shown in tables. In the boys' ward 10 were already immune; of those who were not immune 8 did not develop the disease, 2 developed a marked rise in antibody titre and a positive skin reaction, and 2 developed the disease and gave a positive skin reaction after 16 and 39 days. Essentially similar results are presented for the patients in the girls' ward who were involved in the second outbreak of infection.

D. J. Bauer

KOLARS, C. P. & SPINK, W. W. **Thrombopenic Purpura as a Complication of Mumps.** *J. Amer. Med. Ass.* 1958, Dec. 27, v. 168, No. 17, 2213–15.

This important article draws attention to a hitherto unrecorded complication of mumps—thrombocytopenic purpura. 3 patients, 2 women aged 65 and 27, and a man of 44, were seen within a brief period, all within 2 weeks of the appearance of parotitis. The clinical appearances were characteristic, there was a history of recent contact with mumps in each case, and the complement-fixation tests were positive. The platelet counts were found to be under 25,000. In the 2 female patients the bleeding was controlled by steroid therapy, but there was little improvement in the platelet counts, and splenectomy was performed. The operation failed to produce more than a transitory rise in the thrombocytes, and normal health was only gradually regained. In the male patient, steroid therapy rapidly controlled the orchitis, which was present in addition, and the bleeding did not persist, but a substantial rise in the thrombocytes was achieved only after 3 months of prednisone therapy in varying dosage.

The pathogenesis of this serious complication is not clearly understood, but is likely to be concerned with a state of acquired hypersensitivity rather than with direct invasion by the virus. *H. Stanley Banks*

SILHAR, A. S. & MARU, A. M. **Dihydroergotamine in Mumps.** *J. Indian Med. Ass.* 1958, Dec. 16, v. 31, No. 12, 474–7.

Dihydroergotamine tartrate in a dose of 1 mgm. daily was given intramuscularly to 25 children, aged 9 months to 12 years, in the acute stage of mumps; 6 had 1 injection, 13 had 2, and 6 had 3. As a control group, 25 other children were treated with salicylates and belladonna plasters. In the ergotamine-treated group fever, pain and swelling subsided in 1 day, 2 days and 4 days, respectively, compared with 4 days, 6 days and 10 days in the control group.

A. B. Christie

VYSOKÁ, Běla. **The Epidemiology of Pertussis and Parapertussis.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 2, 196–204, 5 figs. [45 refs.]

Chloramphenicol is of use only in the first 2 weeks of the illness, usually before the whoop develops. Effective field work must concentrate on trying to discover early cases among contacts before they are clinically recognizable. The author claims to be able to do this by bacteriological investigation of contacts and to be able to cut short epidemics by using chloramphenicol in these early cases. He shows that chloramphenicol cuts short the excretion of the organism in patients only if given early in the disease and that patients may cease to excrete under treatment but begin to excrete again when treatment is stopped—sometimes up to the 10th and 12th week. Relapses or reinfection have occurred in patients treated with chloramphenicol even as long as 9 months later.

Parapertussis was very prevalent in Prague in 1956 and took 2 forms—an attack with symptoms similar to pertussis but less severe and lasting only 2–3 days, and an attack with symptoms of bronchitis with a dry irritating non-paroxysmal cough. Only 1/5 of the patients with parapertussis are paroxysmal, 2/5 have the bronchitic type of illness and 2/5 have no symptoms though the organism can be cultured. In pertussis, over one-half have a paroxysmal illness and only a very few have no symptoms. The epidemiological problems involved are therefore quite different, it being difficult to control parapertussis with so many inapparent infections, but easier and more worth while to attempt to control outbreaks of pertussis. *A. B. Christie*

FREUD, P. **Congenital Varicella.** *J. Dis. Children.* Chicago. 1958, Dec., v. 96, No. 6, 730–33, 1 fig. [21 refs.]

A description of a case is given to be added to the list of 14 cases of neonatal varicella (onset within 9 days of birth) collected by the author from the literature. It would seem that infants generally are immune to this disease unless either the mother herself suffers from chickenpox during the last 2 weeks of pregnancy, or she has never had the disease, which, however, is affecting her other children at that time.

In the present instance, the mother developed a chickenpox rash 8 days before the birth of her child. 48 hours after birth the infant's temperature rose and the first vesicle appeared of what, during the following days, became an extensive eruption. Recovery was almost complete in 3 weeks.

None of the new-born infants in the nursery developed the disease, but in the isolation ward to which the baby was transferred on the second day, and in which there had been no case of chickenpox for 3 months, a 4-year-old girl and a 7-year-old boy developed the disease 2 weeks and 16 days, respectively, after the admission of the infant.

J. Pickford Marsden

MARENNIKOVA, S. S. **The Use of the Haemagglutination-Inhibition Test for the Diagnosis of Smallpox.** *Problems of Virology.* London. 1958, v. 3, No. 2, 78–81. [Translated from Russian.]

The author's thesis is that in patients suffering from smallpox the antihaemagglutinin titre rises to a level which exceeds that in recently vaccinated patients and that, therefore, the estimation of this titre may be a useful diagnostic manoeuvre. However, in the 46 cases of smallpox of differing degrees of severity which he quotes the antihaemagglutinin titre, between the 6th and the 60th days of disease, varied widely between 20 and 5,120. In 7 healthy smallpox contacts, 2–4 weeks after vaccination, the antihaemagglutinin titre varied between 0 and 160, generally a much lower figure than in the majority of the smallpox cases. In 2 smallpox patients the titre was shown to rise significantly during the course of the illness.

[The thought that the diagnosis of smallpox might depend on the results of such a test makes at least one clinician shudder.] *J. Pickford Marsden*

CABASSO, V. J., RUESEGGER, J. M. & MOORE, I. F. **Further Clinical Studies with Smallpox Vaccine of Chick-Embryo Origin.** *Amer. J. Hyg.* 1958, Nov., v. 68, No. 3, 251–7, 1 fig.

"As an extension of previous studies, smallpox vaccines of chick-embryo and calf-lymph origin were compared in 3 trials on 4,503 children. Accurate vaccination histories could not be obtained in any of the trials, but most children exhibited old vaccination scars.

"In the first trial, 929 children receiving glycerinated chick-embryo vaccine gave 3·1 per cent primary takes, 35·2 per cent accelerated takes, 60·8 per cent immune responses, and 0·9 per cent no takes, as compared to rates of 3·9, 37·0, 58·2 and 0·9 per cent for the respective types of reactions in another group of 227 children who received glycerinated calf-lymph vaccine on an alternate basis.

"In the second trial, 1,994 children received glycerinated chick-embryo vaccine and 1,962 received glycerinated calf lymph, a total of 3,956 children vaccinated. Positive takes amounted to 87·3 per cent of the first group and 94·8 per cent of the second. This difference is significant but, as pointed out above, some factors other than the efficacy of the vaccine may have contributed to this discrepancy. Upon revaccination with conventional calf-lymph vaccine 1 year later, no difference in response was noted among the two groups of children, indicating a comparable degree of protection afforded by the two types of vaccine.

"In the third trial, on relatively small groups of children, sorbitol-suspended vaccines of chick-embyro and calf-lymph origin were compared with glycerinated calf lymph. Once again, no differences in response were observed. Furthermore, sorbitol gave rise to no abnormal or undue reactions, indicating that it could replace glycerine in the preparation of smallpox vaccine."

BOAKE, W. C. **A Study of Illness in a Group of Cleveland Families. XVIII. Tobacco Smoking and Respiratory Infections.** *New England J. of Med.* 1958, Dec. 25, v. 259, No. 26, 1245–9, 4 figs. [16 refs.]

The incidence and symptoms of common respiratory illness in 51 women and 50 men in 1952–4 are studied in relation to their smoking habits. The illnesses comprise the common cold, rhinitis, laryngitis, bronchitis, non-bacterial pharyngitis and other acute respiratory illnesses of undifferentiated type. No appreciable difference in their incidence was observed between cigarette smokers and non-smokers. On the other hand the infections were more often accompanied by cough in smokers than in non-smokers while sore throat and hoarseness were somewhat less in heavy smokers. [If, however, the 3 grades of smoking be taken into account the association with hoarseness would appear to be extremely doubtful and, as the author points out, in all cases selective factors may influence the comparisons. But on this evidence it certainly seems unlikely that such respiratory infections are materially associated with smoking.] *A. Bradford Hill*

MOGABGAB, W. J. **Recent Developments in Upper Respiratory Disease.** *Amer. J. Med. Sci.* 1959, Jan., v. 237, No. 1, 115–24. [55 refs.]

SAMPAIO, A. & CAEIRO, F. de M. A epidemia de gripe "asiática" em Portugal, 1957. [**An Epidemic of Asian Influenza in Portugal**] *Bol. Serviços de Saúde Pública.* Lisbon. 1958, July–Sept., v. 5, No. 3, 267–359, 3 graphs. English summary.

This is an extensive report describing the epidemiological features of Asian influenza in Portugal. The disease was first observed in Lisbon, during the second week of August 1957. From this time until the end of September, sporadic cases and small outbreaks were observed in several parts of the country. The disease assumed epidemic proportions in late September and the highest incidence for the whole country was reached in late October and early November. The incidence of influenza was of 51·98% among school children and of 29·29% among workers. A death-rate of 12·7 per 100,000 (1,050 deaths) was recorded for the whole population and the age-groups mostly affected were those under 5 and over 60 years old. *H. G. Pereira*

GAN, K. H., MAMOEN, R. & WARSA, R. **Observations on the Influenza Epidemic of 1957 in Djakarta (Indonesia) and on Antibodies to Influenza Virus in Sera from the General Population in Djakarta.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 4, 484–91.

Clinical and epidemiological aspects of an influenza epidemic occurring in Djakarta (Indonesia) from April to August 1957 are described. The clinical picture was typical of influenza and the incubation period was estimated to vary between 12 hours and 3 days. Virus strains identified as Asian influenza were isolated from throat washings of 8 patients. Influenza was also diagnosed by serological methods in 13 out of 16

patients from whom no virus could be isolated. A serological survey carried out in the general population of Djakarta showed absence of Asian influenza haemagglutination-inhibiting antibodies in sera collected on or before May 1957 and increasing numbers of positive sera during the following months.

H. G. Pereira

HARBOE, A., ROST, F., JUUL, K. & MADLAND, Tora. **Percentage of Individuals presenting Antibody to a/Asia/57 after an Influenza Outbreak in a Military Camp in October 1957.** *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 4, 446–52, 1 fig. [15 refs.]

Sera from 223 recruits were collected approximately one month after a widespread epidemic of Asian influenza and tested by haemagglutination-inhibition against an avid strain of influenza A/Asia/57. Serological evidence of infection was observed in 196 (88%) individuals. Positive serological tests were observed in 60 of 63 recruits hospitalized because of influenza, in 91 of 102 recruits recovered from influenza before arrival or with slight influenza symptoms at the camp and in 45 of 58 recruits without symptoms.

Normal inhibitors of haemagglutination were completely removed from the sera by treatment with cholera filtrate but not with trypsin. *H. G. Pereira*

MELLMAN, W. J. **Influenza Encephalitis.** *J. Pediatrics.* St. Louis. 1958, Sept., v. 53, No. 3, 292–7. [21 refs.]

This is an account of illness in 2 children in whom an encephalitic illness supervened on what appeared to be an attack of Asian influenza. There was diagnostic rise of antibody titres in this serum against the Asian 1957 influenza virus. The author reviews the literature relating to the relationship between encephalitis and influenza. *A. B. Christie*

SUGIURA, A., TATENO, I., KITAMOTO, O., KUSHIRO, F. & ISHIHARA, K. **Cerebral Involvement by Influenza. Report of Three Indicative Cases.** *Japanese J. Exper. Med.* 1958, Oct., v. 28, No. 5, 337–44, 1 fig. [28 refs.]

SEAL, J. R. & GUNDELFINGER, B. F. **Efficacy of Immunization against Asian Influenza in the United States Navy.** *U.S. Armed Forces Med. J.* 1958, Dec., v. 9, No. 12, 1720–35, 2 figs.

The efficacy of influenza virus vaccines was studied by an analysis of the records of outbreaks occurring in ships of the U.S. Navy during the 1957 Asian influenza pandemic. The incidence and course of disease in comparable populations exposed to infection before or after the vaccination programme were used as criteria for the evaluation of the degree of protection conferred by different vaccines. Results obtained with 3 batches of commercial vaccines are reported. The first vaccine contained 250 CCA (chick cell agglutinating) units each of Swine, FM1 and Great Lakes 1954 virus strains per ml.; the second was a monovalent vaccine containing 200 CCA units of A/Japan/305/57 strain per ml. and the third was a polyvalent vaccine with 200 CCA units each of Swine, PR301, FM1, Japan/305 and Great Lakes 1954 strains per ml. No evidence of protection was obtained with any of these vaccines. The possible reasons for this failure are discussed and evidence is presented to show that the 2 vaccines containing the Asian strain compared unfavourably with other similar vaccines in regard to antigenicity. *H. G. Pereira*

PECENKA, J., IZBICKÝ, A. & HÁNA, I. K otázce použití hyperimunního konského séra v profylaxi chřipky. [**Hyperimmune Equine Serum in the Prophylaxis of Influenza**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 1, 9–12, 1 graph.

The English summary appended to the paper is as follows:—

"During a smaller epidemic wave of the 'Asian' influenza, 329 persons out of the employees of a greater concern in Bohemia were immunized by the monovalent hyperimmune equine serum against influenza of type A_2 intranasally with a dose 2 × 0·5 ml. Out of these persons, one employee fell ill during the first week. As the first control serum, a polyvalent serum against the types A′ and B (not against A_2) had been applied to 273 persons, out of which 8 persons fell ill. As the second control serum, normal equine serum had been applied to 249 persons, out of which 6 persons fell ill. No serum had been applied to 536 persons, out of which 17 fell ill. In the organization of the whole action, the working method 'double blind test' was applied consistently.

"The obtained results prove the statistically significant effect of the evaluated serum, even if only small numbers have been operated with."

FUKUMI, H., NISHIKAWA, F., MIZUTANI, H., YAMAGUCHI, Y. & NANBA, J. **An Epidemic of Adenovirus Type 3 Infections among School Children in an Elementary School in Tokyo.** *Japanese J. Med. Sci. & Biol.* 1958, June, v. 11, No. 3, 129–40, 2 figs.

An outbreak of pharyngo-conjunctival fever occurring in an elementary school near Tokyo was investigated by clinical and laboratory methods. The outbreak occurred approximately 2 months after an Asian influenza epidemic. Adenovirus type 3 was isolated from throat swabs of 9 out of 20 patients examined and from 2 of the same patients showing conjunctivitis. Evidence of infection by adenovirus type 3 was also provided by the results of serum neutralization and complement-fixation tests performed in acute and convalescent sera from 6 out of the 20 patients. A study of the clinical and epidemiological features of the disease was mainly based on the results of a questionnaire filled in by the patients. Attempts to correlate infection with bathing in swimming pools gave inconclusive results.

H. G. Pereira

NICHOLSON, H. **Drug Treatment of Pneumonia in Adults.** *Brit. Med. J.* 1959, Jan. 17, 162–5.

The treatment of ordinary pneumococcal acute lobar pneumonia is now a relatively simple matter of giving

penicillin, with sedation for a night or two, and taking the usual nursing precautions. But when the whole subject of pneumonia in adults is considered the range of treatment may be very wide and immensely complicated. A good analysis of the difficulties and how to meet them is given in this article, and these, being numerous and many-sided, are difficult to summarize.

Pneumonia is classified into 2 groups: (1) specific pneumonias, (a) bacterial, due to pneumococcus, haemolytic streptococcus, Friedländer's bacillus, staphylococcus, *Haemophilus influenzae* (the latter 2 often working in conjunction with the influenza virus), and *Mycobacterium tuberculosis*, and (b) viral, due to measles, influenza, psittacosis, rickettsiae (especially in Q fever), and other unidentified viruses; (2) aspiration pneumonias, divided into (a) diffuse forms, usually associated with chronic bronchitis, and (b) localized forms due to aspiration of infected material from the upper respiratory tract, *e.g.*, after a severe cold, perhaps with sinusitis, and often associated with lobular or segmental pulmonary collapse. In general the most urgent matter is to determine the causal organism and its drug sensitivities, so that the appropriate (that is, effective and safe) antibiotic can be applied as soon as possible. Hence a specimen of sputum, or alternatively a throat swab, should be sent immediately for examination, and pending the result penicillin should be given, unless a hospital or other penicillin-resistant strain of staphylococcus is suspected, or other organism not susceptible to penicillin. The recommended dosage of penicillin is 500,000 units every 6 hours by injection for 2 doses, followed by 500,000 units by mouth every 6 hours of phenoxymethyl penicillin until the temperature has been normal for 3 days, and thereafter for a few days in half the dosage. If the causal organism is found to be Friedländer's bacillus, streptomycin 1 gm. every 8 hours for 3 days should be given in addition to the penicillin. [Chloramphenicol alone might be even more rapidly effective, but this drug is played down in this article owing to its possible marrow-depressing effect, although in the rare cases of this serious infection its use immediately might be justified on balance of the risks involved.] Where a broad-spectrum antibiotic is indicated, a tetracycline is generally recommended, except in case of drug-resistant staphylococci, when erythromycin combined with chloramphenicol should be tried first, or, in erythromycin-resistant cases, novobiocin.

Useful suggestions are made for the use of sedative drugs, oxygen, antispasmodic drugs, and the corticosteroids. *H. Stanley Banks*

Zanen, H. C. Twee epidemieën van injectieziekten. **[Two Epidemics of Serum Hepatitis]** *Nederl. Tijdschr. v. Geneesk.* 1959, Feb. 7, v. 103, No. 6, 271–6, 1 fig.

The English summary appended to the paper is as follows:—

"From 1951 to 1957, 4,276 cases of infectious hepatitis and 45 cases of serum hepatitis were notified in Rotterdam. In 419 of these cases there had been some sort of medical intervention within 6 months prior to the onset of hepatitis, while no other cases of hepatitis had been seen in their surroundings, so that a diagnosis of serum hepatitis would also have been possible. In that case not 1 per cent., but nearly 10 per cent. of all hepatitis cases would have been due to medical intervention. Classification by age showed that in patients over 40 years old, about 50 per cent. of these hepatitis cases might have been serum hepatitis. By further analysing the types of treatment and the places where this treatment had been carried out, it was discovered that a great number of hepatitis patients had attended at one particular outpatient clinic. A further investigation revealed that during very busy periods the nursing staff of this clinic changed the needle, but not the syringe when drawing blood for determining the erythrocyte sedimentation rate. When a sterile needle and syringe was used for every new patient there were no more new cases of hepatitis.

"After school immunization against diphtheria more inflammatory reactions than usual were reported. In one school abscesses were seen in 6 children out of 77 who had been inoculated; haemolytic streptococci group A type 11/27/44 were isolated from three of these abscesses. One child developed a scarlet fever rash one day after immunization. The abscesses were attributed to accidental contamination of a common filling-needle and inoculation via the so-called anthepa valves.

"The use of a common filling-needle for different injections constitutes a potential danger of infection and is to be condemned."

Negrelli, Z. & Ferrari, M. Aspetti clinici ed epidemiologici di un recente focolaio di epatite virale contagiosa osservato in provincia di Mantova. **[Clinical and Epidemiological Aspects of a Recent Epidemic of Viral Hepatitis in Mantua Province]** *Igiene e San. Pubblica.* Rome. 1958, Sept.–Oct., v. 14, Nos. 9/10, 506–15. English summary (7 lines).

Some observations are offered on an outbreak of virus A hepatitis affecting some of the inhabitants of a 170-acre farm in Mantua province, Italy. The authors point out first that many details of virus hepatitis are still obscure, though it is known that infection is almost always through the digestive tract and is facilitated by the high infecting power of the virus and its resistance to external factors.

The outbreak described affected 12 persons out of 56 in 8 families all living together on the farm. The hygiene conditions were very bad though the water which came from tube wells was examined both chemically and bacteriologically and pronounced potable. Children from 4 to 17 years of age were most affected and the outbreak lasted from October 1957 to January 1958, 93 days in all. 4 of the patients had no jaundice, and all recovered. There was a definite prodromal period of from 5 to 15 days with malaise. Leptospirosis was excluded.

The authors do not consider that either water or milk was responsible and favour the idea of direct contact, a carrier not being excluded, but admit that this hypothesis is not proved. *W. K. Dunscombe*

MASI, A. T., TIMOTHEE, R. A. & ARMIJO, R. **An Epidemic of Parenterally Transmitted Hepatitis in a Civilian Community.** *Amer. J. Hyg.* 1958, Nov., v. 68, No. 3, 258–71, 5 figs. [24 refs.]

During a period of 26 months 181 patients were observed in a district of Puerto Rico. The epidemiological pattern of the disease, as regards time of occurrence, persons involved, and geographical distribution, suggested that injections of liver extract and vitamin B12 given at the local hospital some 3 months before the appearance of jaundice in each case, may have been responsible for the infection. Subsequent enquiries supported this theory. The attack rate of hepatitis in persons who had received these injections was significantly higher, at least over the age of 20 years, than that in the community at large and in a control group who had received other injections. When the number of injections given at the hospital was abruptly decreased, and the technique improved, the outbreak terminated within 7 months.

It had become a common practice at the local hospital to give "an injection" to out-patients for the alleviation of most complaints. A multiple and defective technique was used, whereby one syringe might be used for 30 patients with a change of needles between each. The containers of the medicament could easily have become contaminated while the syringe was being filled. *H. Stanley Banks*

FADEEVA, T. I. **Serum Prophylaxis of Infective Hepatitis in Children's Establishments in Rostov-on-Don.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 3/4, 515–18. [Translated from Russian.]

Although it is not made quite clear in this translation, "serum prophylaxis" appears to mean prophylaxis with gamma globulin, except in institutions where measles convalescent serum had been given to "protect the children from measles or scarlet fever"; in these cases a protective effect was apparently exerted against infective hepatitis as well, but only for a period of 6–8 weeks. Gamma globulin in dosage of 0·2 cc. per kgm. body weight reduced the number of cases of infective hepatitis in contacts to about one-eighth of that in the controls, whereas convalescent measles serum gave only a 4 fold reduction. The dose of convalescent measles serum was therefore regarded as insufficient. It is also concluded (although the supporting data are not clear) that gamma globulin as a prophylactic in contacts is ineffective if injected more than 10 days after the appearance of jaundice in the patient, and that anti-measles serum given 10 days before the appearance of hepatitis in the ward is also ineffective as a prophylactic against hepatitis. *H. Stanley Banks*

WEHRLE, P. F. & HAMMON, W. M. **Absence of Active Immunization against Infectious Hepatitis. Follow-up Study after Administration of Gamma Globulin.** *J. Amer. Med. Ass.* 1958, Aug. 23, v. 167, No. 17, 2062–5. [16 refs.]

Gamma globulin appears to be an effective prophylactic against infective hepatitis. The protection occasionally lasts much longer than could be explained by passive immunity and the suggestion has been made that an attenuated or inactivated hepatitis agent capable of producing active immunity might be present in gamma globulin. The authors tested this hypothesis by studying over a 5-year period the incidence of hepatitis in 3 groups of people—10,794 given gamma globulin as a prophylactic against poliomyelitis, 10,794 given gelatin and 14,155 not given injections. They concluded that there was no evidence of the presence of a hepatitis agent in the batches of gamma globulin used.

A. B. Christie

OGINO, T. **Infectious Mononucleosis in Japan. With special reference to classifying into Sporadic Infectious Mononucleosis and Epidemic Glandular Fever.** *Kobe J. Med. Sci.* 1958, June, v. 4, No. 2, 59–90, 4 figs. [90 refs.]

The author commences by a review of the history of glandular fever and infectious mononucleosis, especially in Japan. Various names were applied to a number of fevers in Japan such as Tokushima fever, Kagami fever, etc., which OHTIWARA *et al.* stated were the same as infectious mononucleosis, though MISAO and KOBAYASHI in 1954 claimed to have isolated a rickettsia from Kagami fever.

In this paper an outbreak of illness among pupils in a primary school in a village with a population of 6,516 is described, which spread to the homes, and eventually most of the people in the village were affected. A feature of the epidemic was its recurrence the following year. The illness was characterized clinically by "marked papillary proliferation of the tongue" and swelling of the submaxillary, submental and cervical lymph nodes. Pyrexia was present in almost half the patients but sore throat, cough, headache, vomiting and pain in the throat were present in only a small number. The liver was enlarged in 26% but there was no jaundice. The severity of the attack was related to the age of the patient, being more severe in young adults than in children and elderly persons.

Laboratory examinations showed the erythrocyte sedimentation rate raised in 4 of the 9 specimens tested; the total leucocyte count was increased in 5 of 11 tested but the degree of lymphocytosis and monocytosis was low. The highest leucocyte count was 15,000 and in only 6 out of the 11 tested was it over 10,000. The differential leucocyte count did not show a very marked increase in the percentage of lymphocytes or monocytes, and although Downey type 1 cells were found in 7 out of 13 patients their numbers were small. Types II and III were not found.

Urine from 27 patients was examined. Diazo and bilirubin tests were negative, urobilogen positive. Serological tests included the Weil-Felix, Widal and Paul-Bunnell tests. In only one case was the Weil-Felix test positive to a titre 1/160, the Widal (typhoid and paratyphoids) was positive in all cases in titres mostly of 1/40 to 1/160. The Paul-Bunnell test gave a titre of above 1/56 in 12 out of 16 instances and rising titres were found in 7. Absorption tests with bovine and guineapig erythrocytes showed complete absorption in all 3 cases tested. In the author's opinion absorption

tests are irregular and indefinite in epidemic cases but regularly positive in sporadic cases.

As already stated, there was a recurrence of the epidemic in the village the following year, which the author considers was due to relapses rather than to fresh infections. He considers relapses are associated with the epidemic form of the disease and not the sporadic. He agrees with KAUFMAN that the aetiological agent may remain in the body and be reactivated by a lowered resistance, excessive fatigue, physical exertion and other factors.

As a result of his experience in this epidemic the author believes that infectious mononucleosis should be separated into 2 types, namely epidemic glandular fever and sporadic infectious mononucleosis.

P. A. Clearkin

GARFIELD, J. & GENTRY, J. H. **Rupture of the Spleen in Infectious Mononucleosis.** *U.S. Armed Forces Med. J.* 1959, Jan., v. 10, No. 1, 91–3. [12 refs.]

"A case of splenic rupture in infectious mononucleosis following abdominal examination is presented. Thirty-one other cases of splenic rupture in infectious mononucleosis have appeared in the literature. These were reviewed, and only one case was found in which abdominal palpation seemed to be of causal significance. The question of hospitalization in infectious mononucleosis, because of the danger of splenic rupture is raised."

KAUHTIO, J., PAATELA, Marianne & RANTASALO, I. Akut bakteriell meningit hos barn. En återblick på 379 fall behandlade under åren 1946–1957. **[Acute Bacterial Meningitis in Children. A Review of 379 Patients treated in 1946–1957]** *Nordisk Med.* 1959, Jan. 29, v. 61, No. 5, 177–80, 3 figs. [16 refs.]

The English summary appended to the paper is as follows:—

"379 children with bacterial meningitis were during the years 1946–1957 admitted to the Children's Hospital, University of Helsinki, and to the municipal Aurora Hospital in Helsinki. The diagnosis was based on the presence of bacteria in the cerebrospinal fluid (by culture in 70 per cent and by smear alone in 14 per cent of the cases).

"N. meningitidis was the causal organism in 21 per cent, Str. pneumoniae in 20 per cent, and H. influenzae in 29 per cent of the cases. Some other bacterium was found to be the disease-producing agent in 14 per cent.

"One-fourth of the patients were below the age of 3 months at the onset of illness, and two-thirds of the total number became ill during their first year of life.

"The gross mortality was about 70 per cent among the children under the age of 14 days, 45 per cent among the ½ to 3 months old, 25 per cent among the 3 to 12 months old, and 16 per cent among children who became ill after their first year of life.

"Well over one-third of the deaths occurred during the first 24 hour period of hospital care, and in view of this fact it is considered that the treatment of the initial shock at the time of admission is quite as important as the institution of specific therapy with antibiotics.

"As a guidance in the choice of a suitable antibiotic the writers recommend, besides examination of direct smears, culture of cerebrospinal fluid and blood before therapy is started. In meningococcal meningitis, sulphonamides and various antibiotics are useful. In pneumococcal meningitis penicillin in massive doses is recommended, and in H. influenzae infection chloramphenicol. The latter drug was also found to be the safest in those patients in whom the causative organism remained unidentified. Intrathecal administration of antibiotics appears to be unnecessary.

"With these therapeutic principles mortality in meningitis due to Neisseria can be kept below 5%, in meningitis due to Str. pneumoniae below 15%, and in meningitis due to H. influenzae at 5 to 10%. With respect to other types of bacterial meningitis the mortality varies, depending upon the disease-producing organism."

CRAGG, J. & BENNETT, Elizabeth F. **Meningococcal Meningitis. A Family Study.** *Lancet.* 1959, Jan. 31, 248–9.

This article gives information on the carrier state and social and housing conditions of 25 families in which a case of meningococcal meningitis occurred during a period of years in which the disease was endemic. The most important point elicited is that the carrier state was significantly higher among the parents of the affected children than among parental controls. No correlation was found between the incidence of the disease and poor social or housing conditions, in contrast with nearly all previous findings among the civilian population. [The authors draw conclusions on these points, and on the seasonal and sex distribution of the disease, which are unjustified because of the paucity of the data, and of their failure to take into account the differences between epidemic and endemic phases of the disease.] *H. Stanley Banks*

BRANCACCIO, G., TEDESCHI, G. & MANZILLO, G. Il trattamento cortisonico endorachideo della meningite meningococcica. (Contributo clinico.) **[Meningococcal Meningitis Treated with Intraspinal Steroids]** *Acta Med. Italica.* 1958, Mar., v. 13, No. 3, 79–80.

At Naples the authors have treated 19 patients (11 males and 8 females) aged between 15 months and 18 years with intraspinal injections of prednisolone. Dosage was 2·5 mgm. daily for children under 10 years and 5 mgm. daily over that age. Penicillin by the usual routes and sulphonamides were also used.

10 patients received steroid + penicillin + sulphonamide, the steroid being stopped at the 5th day; 9 patients received prednisolone only for 5 days and after its suspension the penicillin-sulphonamide treatment. No deaths occurred in the 19 cases although 5 patients were nearly moribund on admission. The hormone definitely influenced the fever and general toxic state favourably; the cerebrospinal fluid became normal more quickly, hospitalization was shorter and there were no sequelae. However, in the 9 cases where the steroid was first used alone meningococci persisted longer and the cerebrospinal fluid took longer to return to normal.

In equal numbers of patients treated with the steroid + penicillin-sulphonamide method against those given penicillin and sulphonamides only, the advantage was greatly in favour of the former combination and the authors consider that this is the best. However, the intraspinal steroid injections must be stopped at the 5th day and treatment carried on with the penicillin and sulphonamide. Blood-stained cerebrospinal fluid does not constitute a contra-indication to intraspinal steroid treatment.

[Some details of the dosages of penicillin and sulphonamides used would have been interesting.]

W. K. Dunscombe

VANDEPITTE, J., BEECKMANS, C. & BUTTIAUX, R. Quatre cas de méningite à flavobacterium chez des nouveau-nés. [**4 Cases of Flavobacterium Meningitis in Newborn Infants**] *Ann. Soc. Belge de Méd. Trop.* 1958, June 30, v. 38, No. 3, 563–70.

The 4 cases occurred in a maternity hospital in Luluabourg, Belgian Congo, in African infants. In all there was a xanthochromic cerebrospinal fluid, the presence of numerous Gram-negative bacteria and abundant culture of strains of flavobacteria, which were proved by antiserum to be identical. 3 of the 4 patients died notwithstanding the administration of streptomycin and tetracycline, both antibiotics to which the micro-organism was sensitive.

The probable source of infection was believed to be the water in which the infants were bathed and it was thought that the umbilicus or mouth might be the portal of entry and that the source of the bacteria was a slime in the rubber tubing attached to one of the taps of the ward washing basin. *J. W. McLeod*

ALLEN, L. & MURPHY, W. R. **Listeriosis.** *Southern Med. J.* 1958, Nov., v. 51, No. 11, 1454–6, 4 figs.

2 cases of listerial meningitis are described, both fatal [see also this *Bulletin*, 1957, v. 32, 1135]: 1 patient was a child aged 9 days, the other was a girl of 12. In both, thick pus was found round the brain especially at the base, and in the baby abscesses were found in spleen, liver, heart, lungs and adrenals. The organism is a Gram-positive rod and was easily seen in direct smears of the cerebrospinal fluid from the baby; it should not be confused with diphtheroids or pneumococci. It was resistant to penicillin, slightly sensitive to streptomycin and fully sensitive to the wider spectrum antibiotics. *A. B. Christie*

MCMATH, W. F. T. **Poliomyelitis Neonatorum with Respiratory Paralysis.** [Memoranda.] *Brit. Med. J.* 1959, Jan. 10, 98, 1 fig.

Poliomyelitis neonatorum is uncommon but highly fatal. A survey by BATES [this *Bulletin*, 1956, v. 31, 498] showed that 58 cases had then been reported, with 21 deaths. The infection can be contracted through the placenta from a maternal infection before delivery, or by the oral route from maternal faecal infection, or during caesarian section from maternal viraemia. Since most cases develop after the sixth day of life, it would seem that the infection is usually contracted at, or after, birth.

McMath has previously reported a case [*Lancet*, 1955, v. 1, 651; this *Bulletin*, 1955, v. 30, 480], and now reports another—a male infant who at 17 days old contracted an upper respiratory infection from the mother; a similar infection had been present 2 weeks earlier in the father and a sibling, who had visited the mother and baby in hospital. Type III virus was isolated from the stools of the patient and the sibling.

The patient had quadriplegia as well as paralysis of the respiratory muscles, but survived after treatment in an infant's alligator-type respirator.

H. Stanley Banks

RAMON, G. Vaccins et vaccinations contre la poliomyélite. Étude critique. [**Poliomyelitis Vaccines and Vaccinations; a Critical Review**] *Rev. d'Immunologie.* 1958, Apr.–June, v. 22, No. 3, 109–35. [Refs. in footnotes.]

Ramon in this long paper discusses the development of vaccination against poliomyelitis in a comprehensive fashion. He points out how the work on poliovaccine has been founded on earlier work on the prophylactic immunization against diphtheria, tetanus and typhoid, for example. He warns against over-confidence in the campaign against poliomyelitis as there are still many factors about which we are uncertain, particularly the duration of the immunity (serum antibodies) which follows poliovaccination. *A. J. Beale*

GUTIÉRREZ VILLEGAS, L. Resultados de la vacuna contra la poliomielitis, tipo Salk, elaborada en México. [**Results of Vaccination Against Poliomyelitis with a Salk-Type Vaccine Prepared in Mexico**] *Gac. Méd. de México.* 1958, May, v. 88, No. 5, 319–31. [10 refs.]

An account is given of the results obtained with poliomyelitis vaccine prepared in Mexico. The virus was of Salk type and contained the P·2226, Y-SK and Léon strains in the proportions of 2 : 1 : 1, in accordance with the prevalence of Type 1 infections in Mexico. Observations made during the administration of 1,055,229 doses showed that the vaccine was well tolerated, and an adequate rise in antibody titre was observed in 120 cynomolgus monkeys and 150 children. The subsequent incidence of paralytic poliomyelitis in 188,932 vaccinated children aged 6 months to 3 years was 0·42 per 1,000, compared with 1·8 per 1,000 in 313,800 unvaccinated children, giving an incidence ratio of 1 : 4·2 in favour of vaccination.

D. J. Bauer

SLONIM, D. & HLOUCAL, L. K tvorbě a přetrvávání protilátek vážících komplement a neutralisujících virus u klíštové encefalitidy. [**The Formation and Persistence of Complement Fixing and Virus Neutralizing Antibodies in Tick-Borne Encephalitis**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 1, 16–25. [13 refs.]

The English summary appended to the paper is as follows:—

"1. The complement fixing antibodies rise quickly in the blood serum of men suffering from tick-borne encephalitis; they culminate in the 4.—10. week after the beginning of the illness; and they decrease so that, after a year, we do not prove them as a rule or we find them in low titres only [4;8]. The maximum titres of positive reactions in the serum are 64 to 128, only uniquely 256.

"2. The virus neutralizing antibodies rise nearly equally quickly, culminate later as a rule, and persist in the blood serum over years after the infection.

"3. The neutralization indexes determined in the serums of convalescent persons by intracerebral titration in white mice vary in their values between 10^2 and 10^4.

"4. The intracerebral neutralization test in white mice decides reliably concerning the specificity of low, indefinite titres determined by the complement fixation test.

"5. The levels of the complement fixing and virus neutralizing antibodies are mutually not quantitatively dependent.

"6. No relation has been found between the gravity of the illness of tick-borne encephalitis and the intensity of the forming of antibodies."

CHUEVA, S. V. **A Study of the Epidemiology of Spring-Summer Encephalitis in the Tartar ASSR.** *Med. Parasit. & Parasitic Dis.* Moscow. 1958, v. 27, No. 3, 308–13, 2 figs. [In Russian.] English summary (5 lines).

Russian spring-summer encephalitis was first recognized in the Tartar Autonomous Republic in 1949, although retrospective examination of case histories has since shown that cases were already occurring in 1932.

Between 1949 and 1956, 506 cases have been notified and an apparent 4-fold rise of incidence has occurred which is probably due to improvement in diagnosis. The annual numbers of cases in different regions of the Republic are shown in a map and a table.

The most severely affected areas are densely crowded, and evidently constitute endemic foci of infection of long standing; the forests are mainly deciduous, and *Ixodes persulcatus*, the vector of the virus, occurs in abundance. The usual seasonal incidence of infection is seen; cases occur between April and August, with a maximum of 57·5% in June, the times coinciding with the periods of activity of the vector. 77·5% of persons affected worked in close contact with the forests and most had been repeatedly bitten by ticks. The disease usually took the meningeal form, but abortive forms were also seen, the poliomyelitic form occurred in 13%, and the biphasic form in 4–5% of cases. Recovery usually occurred without sequelae, but 10 cases (1·8%) were fatal and in 13% there was residual flaccid paralysis of the arms. *D. J. Bauer*

KOKERNOT, R. H., SMITHBURN, K. C., DE MEILLON, B. & PATERSON, H. E. **Isolation of Bunyamwera Virus from a Naturally Infected Human Being and Further Isolations from** *Aedes (Banksinella) circumluteolus Theo.* *Amer. J. Trop. Med. & Hyg.* 1958, Nov., v. 7, No. 6, 579–84. [13 refs.]

Bunyamwera virus was previously isolated from mosquitoes in Uganda [this *Bulletin*, 1946, v. 21, 551] and Tongaland (South Africa) [*ibid.*, 1958, v. 33, 561], but this is the first report of its isolation from human blood taken during a febrile illness. The patient was a mosquito catcher in Tongaland and he was identified by means of finger-prints when his convalescent serum specimen was obtained. He had always resided in the area and was aged 13 years. His symptoms were severe headache, neck stiffness and fever, and his recovery was complete. Blood taken on the first day of the disease was inoculated into newborn mice of which 2 were dead and 5 sick on the second day after inoculation. The agent was filterable: its first 2 passages were non-pathogenic for adult mice but it was readily adapted to them. A *Cercopithecus* monkey inoculated with a large dose circulated virus next day but had no detectable symptoms. Comparison of the virus isolated with the previous Uganda and Tongaland strains of Bunyamwera virus by complement-fixation showed it to resemble them closely. A neutralization test demonstrated a significant rise of antibody in the patient's serum during his illness and that the monkey also developed antibody. In the patient's sera an increase of haemagglutinin-inhibiting antibody from less than 10 to 40 and of complement-fixing antibody from less than 8 to 8 was demonstrated. 3 strains of Bunyamwera virus were also isolated from pools of *Aëdes (Banksinella) circumluteolus*; although non-pathogenic for adult mice at the first passage they were easily adapted. Their identity was confirmed by cross-neutralization tests. *C. E. Gordon Smith*

MUKHERJI, P. S., CHAKRAVARTY, A., SUR, A. M. & JUNNARKAR, R. V. **Encephalitis in Nagpur. Clinical Report with Postmortem Findings.** *Indian J. Child Health.* 1958, Dec., v. 7, No. 12, 968–78, 7 figs.

This is a clinical account of 28 hospitalized cases in an unexplained outbreak of encephalitis in Nagpur in June–July 1958; it was preceded by a high incidence of "hyperpyrexia". There had been severe water shortage in the affected area. Three-quarters of the patients were aged under 8 years. There was a sudden onset with high fever. Coma and convulsions were common and 23 of the patients died. Rigors and vomiting were common, diarrhoea less so. Neck or back rigidity was found in 82%. Chest signs were common. There was moderate leucocytosis but no abnormality was found in the cerebrospinal fluid except raised sugar in 4 of 13 cases. One patient was examined at post-mortem and found to have pneumonitis, myocarditis and meningo-encephalitis. [That all the cases described were of similar aetiology cannot be regarded as established.] *C. E. Gordon Smith*

CHAMBERLAIN, R. W., SUDIA, W. D., BURBUTIS, P. P. & BOGUE, M. D. **Recent Isolations of Arthropod-Borne Viruses from Mosquitoes in Eastern United States.** *Mosquito News.* 1958, Dec., v. 18, No. 4, 305–8. [12 refs.]

"Several isolations of the viruses of eastern and western encephalitis from mosquitoes in the eastern part

of the United States are reported. One isolation of WE was made in North Carolina in 1955 from a pool of engorged *Culex pipiens*. In New Jersey in 1956 two isolations of EE were made from engorged *Culex salinarius* and one from engorged *Culiseta melanura*. Pools of non-engorged *C. melanura* also yielded two isolations of EE and one of WE.

"The possible significance of these isolations is discussed briefly."

PIRÈ, E. Osservazioni epidemiologiche sull'infezione tifoide in Bari. [**Observations on the Epidemiology of Typhoid in Bari**] *Igiene e San. Pubblica.* Rome. 1958, Sept.–Oct., v. 14, Nos. 9/10, 487–95, 3 graphs. [15 refs.] English summary (5 lines).

After having mentioned that the administrative region of Apulia has the highest incidence of enteric infections in Italy, the author points out that for the province of Bari notifications of the enteric diseases show a steady and fairly rapid rise from 1946 to 1954, and in the latter year no less than 1,810 cases of typhoid and 341 of paratyphoid were notified. Points of special interest were the relative resistance of the inhabitants of the city to the disease, as compared with immigrants.

In the city itself (pop. approx. 300,000), from 1952 to 1957, the incidence was highest in the 0–10 age-group and up to 1956 the notifications gradually fell, but in 1957 there was a sharp rise in cases at almost all ages, which was particularly marked (over 50%) in the 0–10 group.

From previous investigations already reported [this *Bulletin*, 1958, v. 33, 935] Pirè considers that as many as 1 in 4 of the adult population of Bari can be regarded as serologically positive. For this state of affairs he blames the low standard of living, the antiquated water supply arrangements, the lack of proper sewerage procedures, and the lack of hospital beds, and points out that, after Rome and Taranto, Bari has shown the greatest post-war increase of population, with a birth coefficient of no less than 29·23%, all of which has caused great overcrowding. He considers that it is the sum of all these factors which is responsible for what he calls the sad primacy of Apulia in typhoid endemicity.

[It is not clear why the notifications for the city and the province did not cover the same period, since although those for the province must of necessity be influenced by those for the city, there is some suggestion of a difference in the progress of the endemic when the 2 are compared. Also no further mention is made of the very great increase in notifications in the city in 1957. A rise of nearly 50% over-all might be thought to warrant some comment.]

W. K. Dunscombe

MASI, A. T., TIMOTHEE, R. & ARMIJO, R. **Epidemiologic Analysis of a Water-Borne Typhoid Fever Outbreak.** *Bol. Asoc. Med. de Puerto Rico.* 1958, Aug., v. 50, No. 8, 295–302, 3 figs.

In this paper there is an account of the investigation of an outbreak of 26 cases of diagnosed typhoid fever which occurred in the period August 24 to September 17 1956 in the city of Ponce (population in 1950 was 99,472) in Puerto Rico. Typhoid organisms were isolated from 9 of the patients and phage typing of 8 of the strains showed that 7 were degraded Vi and 1 a W form.

Of these 23 cases 19 were concentrated in 2 adjacent wards in the centre of Ponce. A description is given of the enquiry which was carried out and of the findings which indicated that the unboiled public water-supply was a factor common to all the patients. Water is supplied from a reservoir "with filtration and chlorination processing facilities" and in addition there are 5 deep wells with automatic chlorinators from which water is pumped directly into the distribution network. There are maps of the water-distribution system and of the location of proved and suspected cases in the city. Evidence was obtained that pollution of the water-supply had been caused by Hurricane Betsy which struck Ponce on August 12 1956 and brought heavy rains and interrupted the electrical power to the deep wells. Water pressure in the city decreased and service was discontinued except for 1 hour in every 8 for some days. On certain days after the hurricane bacteriological tests at routine points were positive for coliforms but some of these reports were never transmitted to the authorities. Later a number of sanitary defects were found in some of the houses. In the discussion it is also mentioned that directly after the hurricane many persons from rural areas sought shelter in the city some of whom may have been typhoid carriers.

M. E. Delafield

VYAS, K. J. **Enteric Fever in Children.** *J. Indian Med. Ass.* 1958, Nov. 16, v. 31, No. 10, 397–400.

This is a clinical account of typhoid fever as seen in 30 children treated in a children's hospital at Bhavnagar, Saurashtra, India. He points out that the disease is rare in infants, in whom it usually gives rise to a prolonged febrile gastro-enteritis, without specific features. In the present series the ages ranged from 4 to 12 years, the sexes being equally represented. The highest admission-rate was in the months of July, August and September, and was correlated with the period of most intense fly breeding.

As was to be expected, the clinical features were often uncharacteristic. The temperature charts showed a great variation in pattern, the fever being continuous, remittent, intermittent or of every form in any sequence. The pulse-rate was proportionate to the temperature in the majority of patients, in 7 there was a relative tachycardia and in only 1, aged 12 years, was there a relative bradycardia. The duration of the fever varied from 20 to 27 days in 50% of the subjects, the range being from 17 to 52 days.

Cough was the next most common symptom and was followed by bronchopneumonia [whether this diagnosis was supported by radiological evidence is not stated] in 5 instances. Constipation was more common than diarrhoea, which occurred only in 3 children. Abdominal pain troubled 5 patients in the early stages of their disease. Headache [an unusual symptom in children] was a marked early symptom in 5 instances. Alteration of mood, from restlessness to delirium, was

indicative of a severe infection: of 7 very restless patients 4 died, while frank delirium terminated in death in 2 more children. The "typhoid state" of coma-vigil was shown by 6 patients at some stage of their illness. Meningeal irritation was evident in 2 patients, one of whom died.

A characteristic exanthem was seen on the abdomen during the second week in only 3 instances [this rarity accords with general experience].

The state of the abdomen proved of little diagnostic aid, for it was described as soft in 15 patients, tympanitic in 7, tumid in 6 and scaphoid in only 2. The spleen became palpably enlarged in only 6 patients and never extended to more than 2 fingers' breadth beneath the costal margin.

Facilities for laboratory investigation were limited. Blood culture could not be carried out, and for confirmation of the diagnosis reliance was placed on the results of the Widal test [but no details are given of titres obtained]. The leucocyte count showed little tendency to leucopoenia, counts being above 5,000 per cmm. in 24 instances, in 3 of the which it exceeded 11,000.

Complications were unusual; they comprised glossitis, stomatitis and parotitis, suppurative otitis media (in 3 patients), nutritional oedema in 4 and consolidation of the lung in 5. In 1 child consolidation of the lung was the presenting sign and justified a diagnosis of "pneumo-typhoid".

The guiding principle of treatment was to give a full bland diet based on rice, mashed potato, lentils, milk, whey, fruit juice and glucose water. A multivitamin preparation was also given. Chloramphenicol was given to 18 children in a daily dose of 50 mgm. per kgm. body weight [duration not stated]: of these 2 died. Of the 12 children to whom antibiotic was not given 6 died. [No criteria of selection are given.]

[This is a clear account of typhoid fever in young, and probably undernourished, subjects, which emphasizes the difficulties of clinical recognition of this disease in childhood.] *J. H. Walters*

LANZO, A. Terapia con prednisone associato a CAF nel tifo addominale. **[Prednisone Associated with Chloramphenicol in the Treatment of Typhoid]** *Arch. Ital. Sci. Med. Trop. e Parassit.* 1958, Oct., v. 39, No. 10, 633–8.

The English summary appended to the paper is as follows:—

"The author has treated 20 cases of typhoid fever with CAF and 20 others with CAF and prednisone, with comparison of the results. Prednisone has not demonstrated particular advantages in light cases; it has given dramatic and very interesting response in cases with serious toxemia."

SHAPIRO, S. E. **Relapses in Synthomycin-Treated Typhoid and Paratyphoid Patients.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 3/4, 542–7. [Translated from Russian.]

This is an account of relapses in a series of 250 cases of typhoid, 40 of paratyphoid B, and 10 of paratyphoid A, treated with synthomycin [apparently synonymous with oxytetracycline]. The number of relapses was 77 (30·4%) in typhoid, and 5 (10%) in paratyphoid. Their frequency was related to the severity of the original attack, to the patients' ages (more frequent in children than in adults), to the season (most frequent in winter), but not to the dosage of, or time of starting, the drug. The Widal reaction [details not stated] tended to be negative or of low titre in the relapsed cases. The dosage of the drug was small (0·05 to 0·075 gm./kgm. daily) and the lowest relapse rate occurred in those who had interrupted cyclical treatment—a primary course of 5–6 days, interval of 5–7 days, and then a second 5-day course. The interval between the primary fever and the relapse tended to exceed the 15-day interval commonly seen in cases treated without antibiotics. In every case the relapse responded rapidly to a second course of antibiotic treatment.

H. Stanley Banks

SCOTT, G. A. **Some Observations on the Epidemiology of a Sonne Dysentery Epidemic—Stirlingshire, 1958.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1959, Jan. v. 17, No. 1, 12–13.

Over a period of 6 weeks between January and March 1958 80 bacteriologically confirmed cases of *Shigella sonnei* infection occurred in a village of 1,300 inhabitants in Stirlingshire. Of these 80, 57 had some diarrhoeal symptoms, the remainder none. 49 of those with symptoms were children in the 0–14 age-group. The number of households where a case of diarrhoea occurred was 33 involving 164 persons all told. Food, water, and milk supplies could not be implicated.

The author discusses probability of infection and clearance rates, and states [rightly] that Sonne dysentery is not a summer disease and that the role of the symptomless excreter must not be minimized.

W. K. Dunscombe

COOPER, G. N. **Shigellosis in Victoria.** *Med. J. Australia.* 1958, Dec. 6, v. 2, No. 23, 770–73. [13 refs.]

While acute bacillary dysentery is rarely encountered in Australia today organisms belonging to the genus *Shigella* are frequently isolated during the routine diagnosis of enteric infections but there is surprisingly little information on the incidence of shigellosis. The present report surveys the incidence of shigella infections in Victoria over the past 6 years but the figures do not include those of patients in mental institutions. These will form the subject of another report. The greater proportion of the organisms isolated was from persons in the urban area.

Only 2 species, *Shigella flexneri* 2a and *Sh. sonnei* appear to be endemic in the state and were responsible for the majority of the cases of shigellosis encountered during the period of the survey. The incidence of shigella infections based on the number of bacteriologically proved cases declined over the period of the examination. *Sh. flexneri* cases appeared to be more sporadic than those of *Sh. sonnei*. In general, infections caused by *Sh. flexneri* 2a were more severe than those produced by *Sh. sonnei*.

The problems presented by shigella infections are not so great as those presented by salmonellae, the total number of shigellae isolated over the 6 years being approximately one-third of the number of strains of salmonellae strains isolated from human patients over the same period, nevertheless it may be considered one of the more common infectious diseases in the State.

P. A. Clearkin

STEIN, H. & SHAFF, G. **Antibiotics in the Treatment of *Shigella* and *Salmonella* Enteritis.** *South African Med. J.* 1958, Dec. 6, v. 32, No. 49, 1161–4. [11 refs.]

It has been estimated that every tenth African child born in Johannesburg dies of an attack of diarrhoea before the age of 1 year [this *Bulletin*, 1957, v. 32, 415].

In Cape Town, gastro-enteritis is the cause of 45% of the deaths of all non-European children of under 1 year of age [*ibid.*, 838].

In the summer of 1954–5, shigella and salmonella organisms were isolated from 29% of 241 consecutive cases of gastro-enteritis admitted to one ward of the Baragwanath Hospital in Johannesburg. It is probable that, under optimal conditions of investigation, these organisms would be isolated from 50% of all cases of severe gastro-enteritis in infants. Since these organisms cause severe diseases with a high mortality, it is essential to determine the most effective antibacterial agent for general use. Investigations carried out in 1954–5 showed chloramphenicol to be relatively more efficient than oxytetracycline or the sulphonamides. This agent, however, is expensive and liable to cause marrow depression. There was also a suspicion that the sensitivity to chloramphenicol of these organisms might be diminishing. For these reasons it was decided that a reassessment of the situation was necessary.

In the summer of 1957–8 therefore all salmonella and shigella organisms isolated were subjected to *in vitro* sensitivity tests to chloramphenicol, streptomycin, neomycin, tetracycline (Achromycin) and sulphatriad. 53 were salmonellae and 92 shigellae, the latter comprising 64 *Sh. flexneri*, 13 *Sh. sonnei*, 8 "Sh. Newcastle" [*Sh. flexneri 6*] and 7 *Sh. schmitzii* [*Sh. dysenteriae 2*]. At the same time all affected patients were placed on treatment with oral chloramphenicol palmitate, 40–50 mgm. per lb. body weight daily for 10 days. Those treated comprised 31 children with salmonella enteritis and 56 with shigella dysentery.

After sensitivity testing lasting 2 months it appeared that streptomycin might be equally as effective as chloramphenicol, and a group of patients were placed under treatment with this antibiotic at a dosage similar to that of chloramphenicol, for the same period. The solution, which was also administered orally, was freshly prepared every 48 hours. Of this second group, 10 were suffering from salmonella and 19 from shigella infections.

All the patients, who were under 2 years of age, were severely toxic and dehydrated, 94% requiring intravenous therapy. Rectal swabs were cultured on completion of treatment, on the occurrence of relapse or prior to a change in treatment.

With regard to the 92 shigella strains isolated, *in vitro* testing showed 74 to be highly sensitive to chloramphenicol, 32 to streptomycin and 23 to neomycin. Moderate sensitivity to chloramphenicol was shown by a further 14, to streptomycin by 49 and to neomycin by 63. Sensitivity to tetracycline was low, only 1 being highly sensitive while 20 were resistant. A disquieting finding was that 88 out of the 92 strains were highly resistant to sulphatriad. These findings applied equally to all types of shigella infections.

Drug sensitivity of the 53 salmonella strains isolated was as follows. High sensitivity to chloramphenicol and streptomycin was seen in 26 instances each, while 32 were highly sensitive to neomycin. Most cultures were resistant to tetracycline and all were resistant to sulphatriad.

On clinical trial with chloramphenicol, of the children infected with shigella strains 73% recovered promptly, 14% died within 5 days of the initiation of treatment and 13% relapsed but recovered on repetition of the same course of treatment. Under treatment with streptomycin, 8 out of 19 (42%) recovered uneventfully, 4 (21%) died and 7 (37%) relapsed. These relapsing patients then received the agent to which their organism had proved most sensitive, in 5 instances chloramphenicol and in 2 neomycin, after which they recovered.

In the case of salmonella infections, 31 patients were treated with chloramphenicol, of whom 23 (74%) recovered uneventfully, 6 (26%) died within 6 days and 2 (9%) relapsed but responded to a subsequent course. A course of streptomycin was given initially to 10 children, of whom 4 (40%) recovered, 3 (30%) died and 3 (30%) relapsed. Of the last, 2 recovered subsequently on neomycin and 1 on chloramphenicol.

Chloramphenicol thus emerged with an untarnished reputation as the drug of choice in salmonella and shigella infections in childhood as seen in Johannesburg, and a comparison with the results obtained in the previous investigation of 1954–5 [*ibid.*, 1956, v. 31, 378] shows that no increased resistance to it has developed in these organisms.

[A careful, convincing and valuable study.]

J. H. Walters

TUBERCULOSIS

SOUTH PACIFIC COMMISSION. Noumea, New Caledonia. **Report of the Conference on Tuberculosis held in Pago Pago, American Samoa, 10–20 November, 1958** [KENNEDY, J., Chairman]. 1958, Nov., 19 mimeographed pp.

26 doctors met in Pago Pago to discuss various tuberculosis problems encountered in American, British, Dutch, Filipino, French and Trust territories in Oceania. Those invited to the conference were specialists from metropolitan countries and tuberculosis and public health officers from the territories.

Epidemiological information is lacking or incomplete in nearly all areas so that the opinions of the Conference are based largely on impressions. The general opinion was that disease patterns and epidemiological conditions vary and in the absence of facts comparison of one territory with another is not possible. Uniform

techniques, especially of tuberculin testing, and uniform statistical methods should therefore be introduced.

It was concluded that the main mode of transmission of infection is by the respiratory route. Overcrowding, bad housing, malnutrition, indiscriminate spitting and other dirty customs and habits play a part in spreading infection, and the Conference felt that environment is more important in pathogenesis than heredity.

Tuberculosis control should be the responsibility of a single authority in any community, and epidemiological studies should be made to determine the magnitude of the problem and the factors which influence it. Attention should also be paid to the possibility of the introduction and spread of bovine tuberculosis.

Methods of diagnosis were discussed. It was generally agreed that all children under 10 years found to be reactors, all persons with hypersensitivity (induration of 16 mm. or more to 5 or 10 TU) and vaccinated persons showing a sudden rise in sensitivity should be X-rayed.

The need for simple efficient techniques for the collection of specimens of sputum and the provision of properly trained staff to examine them was recognized. The great value of radiography is beyond doubt and truly portable and simple apparatus should be obtained. No such equipment was available at the time of the Conference. Every consideration should be given to the protection of patients and operator from excessive radiation, and it was agreed that when possible fluoroscopy should be avoided.

Tuberculosis should be a notifiable disease, and a central register of all patients with active disease should be kept. Compulsion may be necessary to control infectors. Health education of a suitable kind should be introduced into the territories.

Hospital beds are insufficient but very costly to provide; ambulatory and domiciliary treatment should therefore be given priority. Short-term hospital treatment of infectious patients should always be attempted followed by long-term out-patient treatment. The provision of night hostels might help.

Contact examination should be pursued, particularly of those groups for whom the danger of the development of active disease is greatest, *e.g.* infants and adolescents. All non-reactor contacts should be vaccinated with BCG and reactors investigated.

It was agreed that BCG vaccination of all non-reactors in the community regardless of age is valuable and careful post-vaccinal tuberculin testing should be done. Chemotherapy with isoniazid was recommended for recently infected persons but chemoprophylaxis only for contacts. None of these preventive measures should be allowed to lead to the neglect of established and proved public health approaches to the prevention and spread of tuberculosis. *H. G. Calwell*

NORTHERN IRELAND TUBERCULOSIS AUTHORITY [CHRISTIE, D. H., Chairman]. **Twelfth Annual Report Year ended 31st day of December, 1957.** pp. xiv + 63, 3 graphs (1 coloured) & 1 coloured folding map. 1958. Belfast: 27, Adelaide Street.

This annual report is on similar lines to that for 1956 [this *Bulletin*, 1958, v. 33, 20].

The death-rate per 100,000 population from respiratory tuberculosis was 10·72 (10·52) and from non-respiratory 1·79 (1·22). The figures in brackets are those for 1956. The number of new cases notified was 1,155 which is a reduction of 12% on 1956 and is a morbidity rate of 83 (94) per 100,000. Attendances at the 28 chest clinics numbered 71,373 (71,512) and patients whose names were on the Authority's register numbered 13,963 (14,425). There were 4 "contacts" for every new case brought to notice and 88·73% (89·58%) were examined.

The 1,413 hospital beds available are 139 fewer than in the previous year; 106 of these 139 were for respiratory patients and 33 for non-respiratory. There is now no "official waiting list" for a hospital bed: there were 259 vacant beds at the end of the year and 23 patients about to enter them. The Orthopaedic Hospital is used increasingly for the non-tuberculous mainly poliomyelitis.

The Authority administers a domestic help scheme in 2 counties and pays the Welfare Committees for providing it in the rest of the Province.

A noteworthy contribution to rehabilitation is the staffing of a large printing department by ex-patients.

The annual X-ray examination of the chests of school teachers revealed 9 not previously known cases. This is a rate of 1·15 per 1,000 examined. The total number of examinations made by the mass X-ray units was 117,541. The special sessions for persons referred by general practitioners were the most productive.

The number of persons vaccinated with BCG was 29,981. This includes 11,531 infants under 1 year of age. Tuberculin testing prior to vaccination shows that the percentage positive is falling: at ages 10–15 it was 46·3% in 1954 and 25·1% in 1957.

The Authority's total expenditure during the year was £865,235 of which £519,181 was for hospital maintenance, £187,436 for clinics, BCG and domiciliary services and £31,851 for mass radiography.

There is no "special" report this year.

Allen Daley

DUBLIN, L. I. **The Course of Tuberculosis Mortality and Morbidity in the United States.** *Amer. J. Pub. Health.* 1958, Nov., v. 48, No. 11, Pt. 1, 1439–48, 6 charts.

Tuberculosis is in retreat in the United States of America. At the beginning of the century it was the leading cause of death with a mortality rate of 200 per 100,000 which has now fallen to below 8.

The decline has been almost uninterrupted and is now proceeding at increasing speed; females are in a more favourable situation than males and reached the low rate of 5 in 1956. Although the death rate in non-whites is considerably greater than in whites it is declining at a greater rate.

Tables presenting age-specific death-rates for each of the 2 sexes and the 2 races show that in 1914 the rate was highest in infancy, lowest at 10 years, rose to a new peak at 30–40 and declined moderately among males and much more so among females at the older

ages. The figures for non-whites are parallel with those for whites but at a much higher level.

At present the rates for the 2 sexes among the whites are low and differ little up to the age of 35. Among the non-whites the rates for the 2 sexes are also much the same up to the age of 30 but higher than in whites. After this age the rates for males of both races rise to a maximum at the older ages. White males now show higher death-rates than coloured females at all ages over 50. Dublin accepts FROST'S thesis that the present high rates of mortality from tuberculosis in older persons reflect the earlier period of high mortality in their generation.

The history of the change in morbidity is less well documented. Tuberculin surveys show that in earlier years the reactor rate in adults was practically 100%. Current rates are about 35% in adults and about 5% under 10 years. The rate in a group of naval recruits was found to be 3·5%. It rises rapidly with age and varies with geographical location and race. It was estimated in 1952 that there were 56,000,000 persons in the U.S.A. who had been infected by the tubercle bacillus.

About 70,000 new cases of active tuberculosis are reported annually, and it is believed that some 30,000 are not reported. About 1·8 per 1,000 reactors develop active disease every year. This rate varies with sex and age.

Information about the total number of persons with active tuberculosis is not complete; an estimate given is 250,000 of whom 150,000 are known and 100,000 unknown. There are also some 500,000 persons with inactive tuberculosis requiring observation.

Almost one-half of the newly reported cases of active disease are white males; white females provide the lowest number of new cases. The non-white population is only 10% of the total but 25% of the new cases come from the group.

Dublin estimates that the death-rate should probably decline to 1·3 by 1967 and 0·3 by 1975 but others have estimated much higher rates which he does not accept.

Already large sectors of the population have reached what is nearly complete control, *viz.*, white females and the populations of such states as Utah, Idaho, Iowa, Kansas and their neighbours in the Middle West. The knowledge and the resources are available, and a nationally organized effort would lead to complete control of tuberculosis in the U.S.A. in the course of the next 20 years. *H. G. Calwell*

WILLIAMS, R. G. **The Value of Dual Reading in Mass Radiography.** *Tubercle.* 1958, Dec., v. 39, No. 6, 367–71.

An experiment on dual reading of miniature chest skiagrams was carried out during a routine mass radiography survey in Manchester in 1957. The material consisted of 10,000 35 mm. skiagrams which were read simultaneously by 2 independent observers and 576 large skiagrams of 576 patients recalled for further examination, which were read by only 1 of the pair of observers. Cardiac abnormalities were not taken into consideration.

Of the 576 persons recalled the miniature skiagrams had been reported as abnormal in 421 cases by reader A and in 429 by reader B. The recall rate after dual reading was approximately 35% higher than after single reading. The addition of the second reader improved the average yield of radiologically significant shadows by 12% but it also increased the yield of normal shadows by 61% and of non-significant shadows by 42%.

A 1-year follow-up was made of patients referred for further investigation after being missed by one or other of the readers. There were 24 such patients of whom 2 were lost sight of; both had small tuberculous lesions according to the radiological diagnosis but it was extremely doubtful if these were active. Of the 22 who were followed up 15 had pulmonary tuberculosis but the disease was found to be of clinical significance in only 1. Bronchial carcinoma was found in 1 patient; it was inoperable. 1 patient had bronchiectasis which did not require treatment, and 1 had symptomless aspiration pneumonia. The other diagnoses were: hiatus hernia 1, substernal thyroid 2 and basal air cyst 1. These last 3 patients were symptomless and did not require treatment.

A similar follow-up was made of patients referred for further investigation after being detected by both readers. 5 patients presumed to be tuberculous defaulted and 50 of the remaining 79 had tuberculosis. The disease was active and required treatment in 15, it was inactive in 17, and 18 were still under observation but without treatment. Malignant tumours were present in 7; 3 were excised, 1 was treated by radiotherapy and 1 was unsuitable for treatment. There were 2 benign tumours, 2 cases of pneumonia requiring treatment, 14 of bronchiectasis, 2 of hiatus hernia and 2 of pneumoconiosis. The last 18 patients did not need treatment.

It was seen, therefore, that although dual reading demonstrably increased the yield of detection of abnormalities the clinically significant gain was slight. A noteworthy disadvantage of the method is the increase in negative and non-significant recalls. In this trial the increase was over 40% representing approximately 140 additional attendances with consequent unnecessary anxiety and inconvenience for many people. [See also this *Bulletin*, 1955, v. 30, 295.] *H. G. Calwell*

GLASGOW, CORPORATION OF (with the Western Regional Hospital Board in co-operation with Dept. of Health for Scotland & Scottish Information Office). **Glasgow's X-Ray Campaign against Tuberculosis, 11th March–12th April, 1957.** 117 pp., illustrated. 1958. Glasgow C2: City Chambers. [5s.]

This luxuriously produced report is a worthy record of a worthy achievement. It tells how an anti-tuberculosis campaign was planned and conducted and the results that were obtained.

In 1956 the Secretary of State for Scotland announced that a 2-year campaign against tuberculosis would start in 1957. Glasgow was chosen to open the campaign with a 5-week intensive mass radiography survey from

March 11 to April 12. The reason for this choice was that one-fifth of the total population of Scotland is contained in the city (1,083,500) and in 1956 the highest notification rate in any city of the British Isles was recorded there (160 per 100,000). The tuberculosis death rate too was the highest (25).

For 6 months before the opening of the survey publicity of many kinds was used to advertise it and prizes of high value were offered to attract the citizens to the X-ray units. A letter was sent to every household by the Medical Officer of Health inviting every person over 14 years of age to attend for examination.

There were 36 mass radiography units from various parts of Great Britain, and it was thought that if they were fully occupied each would be able to deal with 2,000 persons weekly. The response was however so great that in fact 714,915 persons were examined.

A well organized chest service was essential to the ultimate success of the campaign as the work of the X-ray units would have been nullified if those persons found to have a significant abnormality were not dealt with efficiently and speedily by the chest physicians. The service was therefore modified and adapted to cope with an estimated number of 3,000 patients each and a total of 11,000 contacts in the whole city.

It was recognized that the chest hospitals in Glasgow would not be able to admit all new patients requiring hospital treatment and that patients would have to be sent elsewhere. The bed situation was therefore reviewed just before the start of the survey and provision was made for 1,250 admissions throughout the country.

Pulmonary tuberculosis of certain activity or doubtful activity requiring observation was discovered in 7,053 persons (9·9 per 1,000 examined) of whom 6,511 (10·1 per 1,000) were residents of Glasgow. In addition 1,168 known tuberculous patients were identified. The number of new cases of active tuberculosis (after assessment) was 2,376 from 22% of whom tubercle bacilli were isolated.

In spite of a 50% increase in the number of health visitors only 55,704 of the 80,244 contacts of the new patients attended for X-ray examination The defaulter rate of contacts during or after the survey was 30%.

Carcinoma of the lung, the prompt diagnosis of which was given critical attention, was found in 347 persons of whom 327 were residents. The rate in men was 0·86 and in women 0·21/1,000; in men over 60 it was 3·1.

Final assessment after 3 months showed 2,764 patients with active pulmonary tuberculosis of whom 966 were in hospital and 1,798 were being treated as out-patients. 5,215 persons required observation and there were 3,596 from whom no action was considered necessary. No details are given of the state of the patients with carcinoma at the time of compilation (15 months after the close of the survey).

The total cost of this gigantic effort was £114,269, which is equal to 3s. 2d. for each person X-rayed and £44 11s. 0d. for each new case of active pulmonary tuberculosis discovered—a very rewarding investment in terms both of the individual's wellbeing and the public health. The book itself is worth a great deal more than the nominal sum of 5s. for which it may be obtained.

H. G. Calwell

SEILER, H. E., WELSTEAD, A. G. & WILLIAMSON, J. **Report on Edinburgh X-Ray Campaign, 1958.** *Tubercle.* 1958, Dec., v. 39, No. 6, 339–59, 2 figs.

A mass radiography survey was carried out in Edinburgh in 1958 the aim of which was to include 80% of the adult population, some 300,000 persons. X-ray units from England, Wales and Northern Ireland joined with Scottish units to provide the service; they numbered 27.

7,500 voluntary household visitors were enrolled to visit 150,000 houses in the city and explain the scheme, and in addition 2,500 volunteers were required for reception, clerical, publicity and transport duties.

Press, posters, cinema, sound radio, television, a circus tent (in which 55,000 persons were X-rayed) and the promise of prizes were all used, the last to attract the lazy, the selfish and the careless. The prizes ranged from a £3,000 house, a motor car, a pension of £2 a week for life and household furniture to numerous smaller items.

During the period March 3–28 a total of 295,037 persons were X-rayed of whom 280,663 were residents, and in addition 28,084 residents had been X-rayed otherwise in the previous 3 months. The percentage X-rayed was therefore 84·4. Details of the administrative and technical arrangements by which this impressive result was achieved are given.

Excluding residents X-rayed just before the survey the overall response was 76·6% of those aged 15 years and over; it was highest in young males and lowest in females over 60 years.

10,455 persons were recalled for further X-ray examination (3·5%) of whom 451 defaulted (4·1%). 105 defaulted at the stage of clinic attendance (2·9%). All significant abnormalities are tabulated according to diagnosis and category of patient, *viz.* resident or non-resident, previously known, defaulter, age and sex.

The overall rate of newly discovered active pulmonary tuberculosis was 1·54 per 1,000 (2·17 in males and 1·01 in females); it varied from 3·3 in males over 60 to 0·44 in females of the same age group. The highest rate in females was 1·63 at 35–44 years. There was a much smaller proportion of patients with advanced disease than in all new patients with active pulmonary tuberculosis diagnosed in the ordinary course in Edinburgh in 1957, and the proportion of patients with cavitation was also lower.

194 patients (45·9%) yielded tubercle bacilli. The proportion with sputa positive on direct examination was much lower than in 1957 in both sexes together and in males but not in females. This difference was not explained on the basis of age and sex distribution. There was a steady rise in the proportion of positive sputa in males with age but the converse was found in females.

There were 100 new patients with carcinoma of the lung (0·36/1,000). The rate in males was 0·64 and in females 0·12. The highest incidence was in males over 60 (2·34/1,000).

The authors recommend a campaign of this sort as particularly suitable for communities where tuberculosis appears to be coming satisfactorily under control.

H. G. Calwell

NEUMANN, G. Die Tuberkulosesituation in den Bundesländern und die Bedeutung der Röntgenreihenuntersuchung. [**The Tuberculosis Situation in the Federal German Republic and the Significance of Mass Radiography Surveys**] *Gesundheitsfürsorge.* Stuttgart. 1959, Jan., v. 8, No. 10, 180–82.

Tuberculosis mortality has declined in all provinces of the German Federal Republic but the decline has not been equal throughout the country. The mortality rate in the entire population fell from 6·78 per 10,000 in 1946 to 1·7 in 1957 whereas the rate in different provinces fell from maxima and minima of 8·5 and 6·0 in 1946 to 1·93 and 1·37 respectively in 1957.

The rate of new cases of open pulmonary tuberculosis was 7·2 per 10,000 in 1950 and 4·19 in 1957. The highest incidences in 1950 and 1957 were 9·5 and 6·41 respectively and the lowest 5·8 and 3·13. It is remarked that notifications in Hamburg in 1957 actually rose by 14% from 1956.

The incidence of active closed pulmonary tuberculosis fell from 16·1 per 10,000 to 9·42; maxima and minima by provinces were 33·3 and 11·0 in 1950 and 22·74 and 5·97 in 1957.

The trend is shown in the following table:

Percentage decline since 1950	Mortality	New cases		Known cases	
		Active	Inactive	Active	Inactive
Schleswig-Holstein	38	44	51	21	29
Hamburg	53	33	28	14	15
Lower Saxony	51	46	45	37	29
Bremen	61	41	71	21	32
North Rhine-Westphalia	52	39	38	33	33
Hesse	49	38	46	32	28
Rhineland-Pfalz	46	42	38	7	11
Baden-Württemberg	50	46	39	43	30
Bavaria	42	28	27	21	16
Federal Republic	48	42	41	29	26

The decline in new cases of active disease was greatest in those provinces where mass radiography has been compulsory. This beneficial effect was seen not only in the provinces but also in the comparable cities of Bremen and Hamburg in which, although other factors are of importance, the greater improvement in Bremen is linked with regular mass radiography surveys in Bremen which are absent in Hamburg.

H. G. Calwell

HANSEN, O. G. & RIDDERVOLD, L. Skjermbildefotografering i Norge. [**Mass Radiography in Norway**] *Nordisk Med.* 1959, Jan. 29, v. 61, No. 5, 169–74. [18 refs.]

The English summary appended to the paper is as follows:

"A short survey is given of the mass-radiography organisation in Norway, notably the National mobile mass-radiography service. Since it was established in 1943 up to the end of 1957 this service has carried out well over 4,100,000 X-ray examinations by district mass radiography of the population over 14 years of age. Each year about 350,000 persons are radiographed by means of seven apparatuses, two of which are installed on boats. Since 1948 the mass radiography is combined with tuberculin tests and BCG vaccination. The authorities concerned have the right to call people to these examinations under the Act of 1947 dealing with X-ray examination by mass radiography. They are planned and performed in cooperation with those public health officers and physicians at diagnostic units who are responsible for the follow-up examinations. The films are read at a central office in Oslo, since 1952 by duplicate readings with independent reading by two specialists and control reading by a third specialist who re-examines the films of those persons who by one or both of the first readers have been referred to follow-up examination.

"Mass radiography has been used most extensively in areas where there is a high incidence of tuberculosis. Of the 20 provinces in Norway 14 have been covered by mass radiography twice, 3 three times, and 1 five times. The attendance in per cent of the native population was in the years 1949 to 1957 between 72 and 84% for men, from 80 to 91% for women. In the years 1949 to 1953 between 2.8 and 4.2 per cent. of the mass-radiography cases were referred to follow-up examination. The follow-up showed that 1.3 to 1.5 case per 1,000 was infectious (previously unknown cases 0.7 to 1.2 per 1,000). Suspected active tuberculosis was found in 1.9 to 3.3 per 1,000 (previously unknown cases 1.2 to 2.0 per 1,000). There was good correlation between the mortality from tuberculosis in the individual provinces and the incidence of new cases of active tuberculosis found. The number of infectious cases of tuberculosis was in the older age-groups more than twice as high for men as for women. A corresponding difference was not found for other tuberculous changes in the lungs. Duplicate readings in 1953 of about 267,000 miniature films distributed over 29 readers showed a variation in the frequency of referrals from 3.1 to 12.1%. The difference is, essentially, due to subjective factors. With unanimous reading by three specialists the incidence of infectious cases discovered by follow-up examination was 7.1%, with divergency between the readers 0.8%. Comparison of primary findings by mass radiography may provide data of epidemiological interest, when the influence of subjective factors on the reading of the films can be eliminated or reduced. This is illustrated by the frequency of radiographically observable calcifications in different age-groups in provinces with a high and a low prevalence of tuberculosis, where the difference in the percentage of tuberculin-positive persons after completed mass vaccination can no longer provide a measure of the dissemination of the infection."

BULL. WORLD HEALTH ORGANIZATION. Geneva. 1958, v. 19, No. 5, 759–951, numerous figs. [Numerous refs.] **Tuberculin.**

In spite of standardization, controlled storage and many other measures, variability in the potency of tuberculin remains a serious problem. It is the theme of this issue of the *Bulletin of the World Health*

Organization which is concerned directly with the production, dilution, stabilization and storage of the PPD used in various international projects throughout the world.

The first 3 papers are by J. GULD, K. MAGNUS, M. MAGNUSSON and H. WAALER, and deal with the stability of PPD when diluted for the Mantoux test.

In the first paper (*Stability of Purified Tuberculin in High Dilutions* pp. 765–82) the authors have investigated the effect of storage on the potency of 5 TU dilutions of PPD, RT-19–21. The stock solution containing 1 mgm./ml. (5,000 TU/0·1 ml.) was used within 3–4 months and fresh dilutions were made each month. These were kept in 20 ml. ampoules of brown glass in the refrigerator or incubator, protected from light.

879 Danish children aged 7–14 years were tested by intracutaneous injection after they had been vaccinated with BCG. 8 dilutions stored for 1–8 months respectively at 2°–4°C. and 20°C. and 3 dilutions stored for 1–3 months respectively at 37°C. were used and compared with a fresh dilution (*i.e.* one stored at 2°–4°C. for not more than 11 days).

The children's reactions were read after 3 days and measured. It was found that there were marked differences with dilutions prepared at different times apparently unrelated to temperature and duration of storage. There were also differences in potency between the contents of ampoules filled with the same dilution and stored at the same temperature.

Similar tests were made in vaccinated guineapigs. The results did not give a clear picture of the effects of storage. There was a tendency towards reduction in potency with increased length of storage at all temperatures but the significance of the experimental data was reduced by large irregular variations just as in the study in children. Despite the very many tests carried out only a very rough estimate of the effect of storage could be reached, and the unsystematic variations found could be erroneously interpreted as effect of storage.

In the second paper (*Adsorption of Tuberculin to Glass* pp. 783–98) the authors investigate the possibility that the unsystematic variations described might be due to adsorption of tuberculin on to the glass of the ampoule. Such adsorption has been described by several authors in different connexions.

If there is adsorption of tuberculin it should be possible to elute tuberculin-active substances from ampoules which have contained tuberculin. Such ampoules were filled with phosphate-buffer diluent which was used to test vaccinated guineapigs and no significant activity was found. When, however, 0·02% of Tween 80 was added to the diluent marked activity was demonstrated. This was clear proof that tuberculin had been adsorbed to the glass.

In another series of experiments an attempt was made to measure the degree of adsorption and relate it to the quantity of tuberculin and the area of glass with which it was in contact. It was found that when 1·5 ml. of a strong tuberculin was stored in a 20 ml. ampoule tuberculin produced a weaker reaction than did a dose of weak tuberculin which occupied the whole ampoule. Adsorption seemed to increase with rise in temperature and to depend to some extent on the degree of dilution and to be influenced by a physical factor. For example, it was reduced by shaking a partly filled ampoule.

In the third paper (*Diluents for Stabilization of Tuberculin* pp. 799–828) the following tuberculins were used: RT 19–21, RT 22, RT 23 and 23p, PPD–S and OT. Diluents used were physiological saline, isotonic phosphate buffer and boric-acid sodium-borate buffer with and without gum arabic. Stabilizing agents used were: agar, Cetavlon [Cetrimide], dextran, gelatin, gum arabic, human albumin, peptone, sodium laurylsulphate and Tween 80. The biological activity of the tuberculins was again determined by testing vaccinated guineapigs. Details of the experimental studies and their results are given.

It was found that the tuberculin reactions obtained with a given dilution of tuberculin were highly dependent on the diluent used. In the case of the Danish tuberculin RT reactions of increasing size were obtained in the following ascending order: dextran in buffer, saline, buffer-saline, buffer with gum arabic, buffer with protein and buffer with Tween 80. The best results were obtained with Tween 80, and a concentration of 0·05% sufficed. There was no evidence of sensitivity to Tween 80 itself; another advantage it possessed was that it reduced the frequency of bullous reactions and appeared to increase the specificity of some tuberculins.

No conclusion was reached about the mode of action of the stabilizing agents but it appeared reasonable to assume that prevention of adsorption on to glass was concerned.

The fourth paper (M. MAGNUSSON and M. WEIS BENTZON) was entitled *Preparation of Purified Tuberculin* RT 23 (pp. 829–43). It deals with the preparation of a new PPD which was issued for use in July 1958.

7 different virulent strains of *Mycobacterium tuberculosis* were cultured on a modified Sauton medium. Biological activity of the 95 different batches of PPD produced was tested in vaccinated guineapigs. All batches were found to be satisfactorily potent but 18 had to be excluded because of precipitation in stock solutions.

The last paper (J. GULD, M. WEIS BENTZON, M. A. BLEIKER, W. A. GRIEP, M. MAGNUSSON and H. WAALER) is entitled *Standardization of a New Batch of Purified Tuberculin* (pp. 845–951). It deals with the extensive biological assays of PPD RT 23 which were made.

One aim was to standardize the new product against the International Standard for PPD-S and another was to compare it with RT 19, 20, 21 and RT 22, which are already widely used throughout the world. A further part of the study concerned the relative potency of RT 23 with and without Tween 80.

Intracutaneous testing was used throughout both in guineapigs and human subjects. In order to provide a large range of variety the animals were sensitized by infection with virulent human tubercle bacilli, BCG or killed avian tubercle bacilli. The human groups tested included tuberculous patients, army recruits and schoolchildren in Denmark, schoolchildren in Nigeria and villagers in Mauritius.

The results varied according to the type and level of

sensitivity in the group tested. The correspondence between RT 23 and the International Standard was about 2 : 1 in vaccinated persons, and 1 : 1 in natural reactors; RT 23 in a diluent containing Tween 80 produced larger reactions than when Tween 80 was not added. Although equal in size, reactions to tuberculin containing Tween 80 were less indurated and less often bullous. Accentuation of the reaction when Tween 80 was present was only seen in subjects with high tuberculin sensitivity.

There were differences between the results in human subjects and guineapigs so that RT 23 without Tween 80 produced more feeble reactions than PPD-S in vaccinated guineapigs and stronger reactions in schoolchildren and army recruits.

The new batch of 500 gm. of tuberculin, RT 23, corresponds to a total of 33,000,000,000 doses of 0·00002 mgm. This quantity will suffice for many years. If 0·00002 mgm. of RT 23 is considered equal to 1 unit of the International Standard PPD, then 0·00006 mgm. of RT 23 in buffer diluent without Tween 80 or 0·00002 mgm. of RT 23 in buffer solution with Tween 80 should correspond fairly well to 3 TU of PPD-S, to 5 TU of RT 19-20-21 and perhaps to 6 or 7 TU of RT 22. The authors are confident in proposing that these doses of RT 23 be used instead of the " 5 TU " test used at present. *H. G. Calwell*

MITCHELL, F. K. & JACKSON, F. I. **'Heaf' Multiple Puncture Tuberculin Test. A Comparison with Intradermal Tuberculin P.P.D. in the Cape Coloured Subject.** *South African Med. J.* 1959, Jan. 3, v. 33, No. 1, 10–12, 1 fig. [11 refs.]

Tuberculosis is the major public health problem in the Union of South Africa, and despite the progress made in treatment the incidence of the disease among the Cape Coloured section of the population of the Western Cape Province has remained high. It was therefore decided to introduce BCG vaccination on a wide scale.

During a visit to Northern Ireland in 1956 Mitchell was greatly impressed with the potential advantages of the Heaf test for tuberculin surveys under conditions such as those found in the Cape Province but before introducing it a trial of its reliability in the population to be tested was made.

180 apparently healthy schoolchildren of both sexes aged 10–15 years were tested simultaneously by the Heaf and Mantoux methods; 156 completed the tests. The Heaf test was done with Protoderm containing PPD, 2 mgm./ml., equivalent to 100,000 TU of OT per ml. The Mantoux test was done with first and second strength PPD (1 and 250 TU respectively).

Both reactions were read at 48 hours and all subjects showing a negative reaction to 1 TU (5 mm. or less) were tested with 250 TU. On the 5th day (72 hours after the second test) the reactions were read again, and finally on the 7th day the Heaf reactions were read a third time. The positive Heaf reactions were assigned to 4 groups according to Heaf's classification. Doubtful reactions were seen, a significant proportion of which became definitely positive at succeeding visits. Mantoux reactions were measured.

Every positive Heaf reaction remained positive throughout the period of observation. Of 15 doubtful readings at 48 hours 5 were definitely positive at 72 hours and remained so at the 7th day. The remainder were obviously negative on the 7th day. 3 children who were negative at 72 hours were positive on the 7th day. The number of 4th degree Heaf reactions was small (8) and none was troublesome.

In comparing the Heaf reaction and the Mantoux reaction to 1 TU it was found that all subjects showing a positive reaction of 6 mm. or more to the Mantoux also showed a positive Heaf reaction. On the other hand, of the 108 subjects who failed to react to 1 TU (5 mm. or less) 37 showed a positive Heaf reaction at 7 days.

Comparison of the Heaf and Mantoux reactions to 250 TU in 108 children who were negative to 1 TU showed that all who reacted to 250 TU also reacted to the Heaf test. Of the 73 subjects showing a negative reaction to 250 TU at 72 hours, 2 showed a positive Heaf at 7 days; these 2 children had reactions of 4 mm. and 5 mm. respectively to the Mantoux test but were recorded as non-reactors by the criterion in use.

As a result of this trial it was concluded that the Heaf test could be regarded as being as reliable as the Mantoux test with 250 TU, and " it is felt that the Heaf test can now be accepted as both effective and safe in the Cape Coloured group ". *H. G. Calwell*

KUPER, S. W. A. **Sensitivity to Human and Avian Tuberculin among Africans in the Union of South Africa.** *Tubercle.* 1958, Dec., v. 39, No. 6, 380–7, 4 figs.

In this investigation sensitivity to human and avian tuberculin was compared in groups of healthy African schoolchildren and adult African patients suffering from pulmonary tuberculosis. The Mantoux test was used with 1 TU of human and avian tuberculin (PPD).

Reactions were read 48–72 hours after injection and if there was a negative reaction (5 mm. or less of induration) the tests were repeated with 10 TU, read and measured as before and if again there was a negative reaction doses of 100 TU were given. All tests were given and measured by the same person.

The first school presented 727 boys and girls aged 10–19 years, an entirely rural group, and the other 474 boys and girls aged 2–6 years, an urban group in an industrial slum. In both groups combined the reactor rates to 1 TU of human and avian tuberculin were 29 and 41% respectively; increasing the dose to 10 TU gave total reactor rates of 42 and 60% respectively. Of those children who did not react even to 100 TU human tuberculin failed to elicit a reaction in 312, whereas avian failed in only 144. It was seen that avian tuberculin was more successful than human in eliciting reactions in healthy subjects.

In view of the substantial differences found in the degrees of sensitivity at the 2 schools and between children of different broad age-groups within these schools it was not considered legitimate to pool the results and they were analysed separately.

In the rural school sensitivity to avian tuberculin was apparently greater at all dose levels. In the older children the reactor rate to avian tuberculin was very similar to that of the younger children at each dose level but the reactor rate to human tuberculin rose with increasing age. In the young sensitivity to avian was greater than to human tuberculin and was probably acquired at an earlier age.

In the urban school also avian tuberculin was more efficient at eliciting reactions than human tuberculin, but this greater sensitivity to avian was hardly discernible at 1 TU level. With low-grade sensitivity, however (needing 100 TU to elicit reactions), avian tuberculin was seen to be more successful than human. The higher level of sensitivity seen in the rural school may have been due to the higher average age of the children there.

Of the 480 tuberculous adults who were available for the first reading 95% reacted to 1 TU of human tuberculin and over 99% to 10 TU; the reactor rates with avian tuberculin were 85 and 97% respectively and almost 100% reacted to 100 TU. It was thus found that in patients with pulmonary tuberculosis [presumably active] human tuberculin was more successful in eliciting the high degree of sensitivity that is detected by very small doses.

A statistical note is given on the problem of measuring tuberculin reactions and the method used here.

The findings are taken to suggest the existence in 2 localities of South Africa of "non-specific" tuberculin sensitivity. [See also this *Bulletin*, 1953, v. 28, 327.]

H. G. Calwell

MANCHANDA, S. S., BAWA, Y. S. & BHATIA, J. L. **Tuberculosis in Children (a Preliminary Report of 215 Cases).** *Indian J. Child Health.* 1958, Dec., v. 7, No. 12, 938–50, 9 figs.

This paper deals with 215 children who were admitted to the paediatric wards of V. J. Hospital, Amritsar, from 1955 to 1957, with symptom-producing tuberculosis. An unduly low proportion of skeletal tuberculosis occurred as many of them were dealt with in the orthopaedic department. Generally speaking the occurrence of various features was similar to that found elsewhere. The most notable feature is the low incidence of erythema nodosum, and the rather high incidence of gastro-intestinal symptoms. The main interest of the paper lies in the possibility it affords of comparing the features of tuberculosis in Indian children with similar groups in other countries.

F. H. Young

CAPEL, L. H. & RICHARDS, W. F. **Transient Rounded Lesions following Tuberculous Pleural Effusion in Children.** *Tubercle.* 1958, Dec., v. 39, No. 6, 388–93, 4 figs.

The rounded shadows which appear in films taken of children's chests after pleural effusions have intrigued most of us. This article examines 21 patients in whom, out of 211 children, these shadows (27) were observed. The patients were followed up for an average of 27 months. 17 lesions were in contact with the medial edge of a resolving effusion, and 10 were apparently isolated. By use of lateral films and tomography 21 were considered to be definitely in the pleural cavity. Some evidence of the shadowing persisted for an average of 6 months. All eventually disappeared leaving occasionally a fleck of calcium, without any clinical effect on the patient.

Comparison is made with the localized effusions reported in heart failure.

It is concluded that most, if not all, of these shadows are small encysted pleural effusions. *F. H. Young*

LINCOLN, Edith M. & ADIAO, A. C. **Late Discharge of Tubercle Bacilli in Primary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 31–40, 1 fig. [20 refs.]

"The significance of the excretion of tubercle bacilli in children six months old or more after the onset of primary tuberculosis has been investigated by a review of the literature and of the experience in the Chest Clinic of the Children's Medical Service of Bellevue Hospital between March, 1947, and July 1, 1956.

"Tubercle bacilli were cultured from gastric or bronchial fluids six months to more than twenty-five years after the initial diagnosis of primary tuberculosis in 44 patients. No significant roentgenographic changes accompanied the late excretion of tubercle bacilli. Twenty-seven patients had endobronchial disease proved by endoscopy, and an additional 8 had roentgenographic or bronchographic findings suggestive of previous endobronchial involvement. Foci of tuberculosis draining into the upper respiratory tract, usually in tonsils or adenoids, were found in 11 of the 44 patients."

CHRISTENSEN, F. & NIELSEN, J. A. **Chemotherapy of Pulmonary Tuberculosis. The Primary Effect of Combined Specific Chemotherapeutical Treatment as revealed at the Examination of 105 Patients in a Danish Sanatorium.** *Acta Tuberculosea Scandinavica.* 1958, v. 36, Nos. 2/3, 73–82.

This article tries to give some idea of the prognosis after drug treatment applied to various types of pulmonary tuberculosis. It reports the results on 105 consecutive patients who satisfied certain criteria, especially that they had not previously received antituberculous drugs. They were given isoniazid, usually with both streptomycin and PAS, and occasionally with one or the other. They were grouped according to the estimated chronicity and extent of the disease, radiologically with or without cavitation. All patients were treated for a minimum of 3 months. Two-thirds were treated for 3 to 6 months, and rather more than one-quarter for 6 to 9 months; a few a little longer.

They were classified as infiltrative A; fibrotic C; and the mixed B. At the end of treatment 91% in type A showed improvement, considerable or moderate; in type B 81%; and in type C 17% (in none of these was the improvement considerable). In type A cavity closure occurred in 53%, type B 30%, but in type C cavity closure did not occur in any of the 9 cases. In all,

the results were better when treatment was continued for more than 6 months than when it was given for 6 months or less. There was very little difference between the various types from the point of view of sputum conversion; the authors claim that the type of disease was more important than its extent in prognosing the likely effects of adequate drug therapy.

F. H. Young

COHEN, S. S., YUE, W. Y. & TSAI, S. H. **Comparison of Toleration, Absorption, and Clinical Efficacy of Several Para-Aminosalicylic Acid Preparations in Three Hundred Tuberculous Patients.** *Amer. Rev. Tuberculosis.* 1958, Dec., v. 78, No. 6, 899–905, 3 figs. [10 refs.]

Excellent though PAS is in the prevention of the development of organisms resistant to streptomycin and isoniazid, it suffers from the disadvantages of being an irritant to the gastro-intestinal tract. Many modifications are on trial to obviate this, but doubts have been expressed about their efficiency. In this paper comparison is made between calcium, sodium and potassium PAS, and Rezipas, which is an anionic exchange resin to which PAS is adsorbed; it contains 50% of para-aminosalicylate. In the trial, 4 doses of 6 gm. were given (= 3 gm. PAS) and compared with 3 gm. of the others, 4 times a day, providing 2·16, 2·64 and 2·01 gm. PAS per dose respectively. Isoniazid in daily doses of 4 to 5 mgm. per kgm. of body weight was given. For studies of tolerance and absorption 300 patients were divided into 4 groups, and of these 155 were selected for trial of clinical efficiency, or terms of efficiency in prevention or postponement of development of resistance.

The results were as follows:—

Incidence and Severity of Gastro-intestinal Symptoms (300 Patients)

	Number of Patients	Symptoms Absent %	Mild Symptoms %	Moderate Symptoms %	Severe Symptoms %
PAS-resin complex	99	52·5	38·4	9·1	0
Potassium PAS	49	16·3	30·6	49·0	4·1
Calcium PAS	81	34·6	39·5	19·7	6·2
Sodium PAS	71	38·1	36·6	21·1	4·2

Satisfactory, though varying average serum concentrations were obtained with all preparations, but in the case of Rezipas low levels were found in isolated cases.

The percentage of patients who still had positive sputa at the end of 12 months was so low that it is assumed that all preparations were adequate to prevent the development of resistant organisms.

Radiologically there was no significant difference between the results obtained by each of the preparations.

The authors conclude that Rezipas is a preparation which is safe to use, and causes less gastro-intestinal disturbance than the others. [This is a very useful piece of work.]

F. H. Young

BARTMANN, K., VILLNOW, J. & SCHWARZ, C. **Acquired Resistance and Isoniazid Medication.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 97–101. [24 refs.]

"An investigation has been carried out to discover whether development of immunity is possible during prophylactic isoniazid treatment in guinea pigs infected with tubercle bacilli and to what extent it depends upon the infecting dose and the type of treatment. Immunity has been measured in terms of protection against a small challenge dose with a highly virulent strain. It was found that after treatment of a massive infection with isoniazid (10 mg. per kg. twice weekly every third or fourth day, subcutaneously) immunity was demonstrable which must have been developed during therapy. It was somewhat less effective than that following BCG vaccination. If the same virulent primary infection was treated with isoniazid (10 mg. per kg. six times weekly), weaker immunity developed corresponding in degree to that produced by a progressive untreated minimal infection. In a minimal infection prophylactically treated with isoniazid (10 mg. per kg. twice weekly), considerable interference with the immunizing process was observed, i.e., only some of the animals became immune and were less protected than would be the case in a progressive minimal infection. Generally, the immune animals of the minimally infected group did not show signs of tuberculosis at the site of primary infection after therapy. This seems to indicate that under the conditions of the experiment, interplay between chemotherapy and the development of immunity prevented the appearance of 'open' tuberculosis."

CUTHBERT, R. J., DRIMMIE, Alison M. T. & URQUHART, K. R. **A Study of "Tebafen" in Chronic Pulmonary Tuberculosis.** *Tubercle.* 1958, Dec., v. 39, No. 6, 359–66. [20 refs.]

The use of the thiosemicarbazones in the treatment of pulmonary tuberculosis was popular in Germany after World War II. One of these, a combination of isoniazid and nicotinaldehyde thiosemicarbazone (TSC) —trade name Tebafen—was tried on 25 sputum positive patients. The organisms were all sensitive to Tebafen, but partial resistance to isoniazid was present in 11. The dosage was 300 mgm. of Tebafen daily, equivalent to 240 mgm. isoniazid and 60 mgm. TSC. All patients underwent their treatment at home; 20 completed 6, and 10 completed 12 months' treatment. The patients had advanced disease. Clinical improvement occurred in 21, but in only 3 was definite radiological improvement noted. Sputum was rendered negative in 6 patients at the end of 6 months, and 8 at the end of one year. 11 patients had developed resistance to isoniazid at the end of 12 months. As Tebafen causes less gastro-intestinal disturbance than para-aminosalicylic acid, it may be useful as an alternative to isoniazid and PAS.

F. H. Young

BACHMAN, H. & FREUND, J. **Report on the use of Isoniazid and Cycloserine in 84 Cases of Pulmonary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 87–9.

"A series of 84 patients with pulmonary tuberculosis have been treated with isoniazid and cycloserine for periods as long as fifteen months. Most of the patients had advanced chronic disease which had received the prior benefit of other drug combinations, including isoniazid in practically every case. Some of the patients had received compression or resectional surgery. In reviewing the results, a significant improvement was observed in a gratifying percentage of the patients. Reversal of infectiousness occurred in a satisfactory number of the patients; roentgenographic improvement was observed in a fair percentage; many patients showed improvement in general well-being and appetite; and there was a frequent reduction in cough and expectoration. Complicating side effects have been few and mild, despite the fact that the series included several diabetics and alcoholics. From this clinical experience, it is concluded that a regimen of 500 mg. of cycloserine and 300 mg. of isoniazid daily, in two equally divided doses, is a valuable regimen for use in patients who still have active disease despite treatment with one of the standard regimens."

STAHLE, I. **Cycloserine and Viomycin in Combined Treatment of Pulmonary Tuberculosis. A Comparative Study.** *Acta Tuberculosea Scandinavica.* 1958, v. 36, Nos. 2/3, 83–97. [69 refs.]

Where a patient's tubercle bacilli are sensitive to the standard drugs little difficulty is likely to occur with drug therapy; but where resistance is present the doctor has to fall back on the drugs which are less proven in efficiency and likely to be more toxic. This article deals with a combination of cycloserine and viomycin. 28 patients received cycloserine and isoniazid, 30 cycloserine and viomycin, and 34 PAS and isoniazid. The conditions of the patients seem to have been fairly comparable, and with 2 exceptions their bacilli were normally sensitive to all drugs tried. The dosage of the cycloserine was 0·5 gm. daily, given in 2 doses, and viomycin 1 gm. intramuscularly every 2 days. At the end of 3 months the cycloserine and viomycin group had done at least as well as the other 2 groups on a very fair assessment. No appreciable toxic reaction to either drug occurred, and in nearly all the 92 cases tubercle bacilli were not cultured in the sputa. This is an interesting paper and will repay careful reading.

F. H. Young

SCHWARTZ, W. S. & MOYER, R. E. **Cycloserine and Viomycin in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 90–93.

"Cycloserine and viomycin in a dosage of 0.5 gm. daily and 2 gm. twice weekly, respectively, given to 71 tuberculous patients who were treatment failures proved to be a useful regimen. This treatment may well be used as a second line of defense in patients for whom other chemotherapy is no longer effective. It is recommended, however, that audiograms or other careful hearing examinations be done in at least monthly intervals during treatment with this regimen."

BIRKELAND, K. & NISSEN-MEYER, S. **Pyrazinamide and Cycloserine in the Treatment of Pulmonary Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1958, v. 36, Nos. 2/3, 98–109. [13 refs.]

This paper gives short accounts of the present knowledge of pyrazinamide and cycloserine in the treatment of pulmonary tuberculosis. It then compares the effects of 3 months' treatment with pyrazinamide, 40 mgm. per kgm. of body weight, and cycloserine, 0·5 gm. daily (the few who weighed more than 75 kgm. received 0·75 gm.) in 3 doses on 17 patients, with that produced by the same dose of pyrazinamide alone on 13. The patients were all advanced cases and were resistant to at least 2 of the standard drugs. 14 of the first, and 10 of the second group completed treatment. Decrease in the size of cavities was a little in favour of the combined therapy group. At the end of 3 months 62% and 30% respectively of the smears were negative for tubercle bacilli, and cultures were negative in 58% and 17%. The incidence of toxic phenomena is given; all were reversible.

The conclusion was that the combined therapy was somewhat more efficient than pyrazinamide alone, but complications were more frequent. It was thought that the combined therapy was useful in some cases, especially before operation where acute spread of disease had occurred.

F. H. Young

TOGURI, E. & ATWELL, R. J. **Cycloserine combined with Pyrazinamide in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, Dec., 78, No. 6, 927–31. [Refs. in footnotes.]

The article reports a trial of a combination of cycloserine and pyrazinamide on 25 patients. They all had bacilli resistant to streptomycin, PAS and isoniazid, and had advanced disease. The patients were treated for 6 months with cycloserine, 250 mgm. every 12 hours, and pyrazinamide, 1 gm. 3 times a day. 20 completed the course (2 died of massive haemoptyses, 2 of pulmonary insufficiency, and in 1 severe urinary infection led to the abandonment of treatment). Toxic symptoms were slight, mainly headache and drowsiness, and seldom persisted after 14 days. In 9 patients tubercle bacilli disappeared; usually this occurred by the end of the third month if it was going to take place. 8 patients showed some radiological improvement. The serum concentration of cycloserine was not higher in those patients for whom negative cultures were obtained. Nearly all patients had bacilli resistant to 20 μgm., but susceptible to 80 μgm., cycloserine at the start of treatment, and only 2 had lost the susceptibility at the end of treatment.

The number of cases reported is small, but the low incidence of toxic manifestations is interesting.

F. H. Young

ALLISON, S. T. **Pyrazinamide in Low Dosage in Combination with Isoniazid or Para-Aminosalicylic Acid in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1959, Jan., v. 79, No. 1, 102–4.

"A group of 164 previously untreated patients were treated by three drug regimens. One hundred and thirteen of these patients received 1·5 gm. of pyrazinamide daily as one of the companion drugs. The overall incidence of hepatic toxicity was 6·2 per cent as judged by liver function tests, whereas the incidence of jaundice was 0·88 per cent. There were no deaths from drug toxicity.

"Pyrazinamide is a dangerous hepatotoxic drug which should be used only in patients whose tubercle bacilli are resistant to the less toxic drugs. Pyrazinamide is effective and may be life saving, so that the possible development of hepatitis constitutes a calculated risk, which is lessened to a considerable degree by frequent liver function tests."

KANAI, K. **Recent Advances in Experimental Research of Tuberculosis Chemotherapy in Japan: a Review.** *Japanese J. Med. Sci. & Biol.* 1958, June, v. 11, No. 3, 87–107. [Numerous refs.]

IONESCO-MIHĂIEŞTI, C., DÂMBOVICEANU, Aristia, DUMITRESCO, Maria, GANCEVICI, G. & OPRESCO, C. C. Sur la vaccination contre la tuberculose: essais expérimentaux comparatifs d'immunisation des cobayes par le B.C.G., le Vole bacillus et des vaccins "synthétiques". [**Concerning Immunization against Tuberculosis: Comparative Experiments on the Immunization of Guineapigs by means of B.C.G., the Vole Bacillus, and "Synthetic" Vaccines**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, June, v. 17, No. 2, 221–35, 3 figs. [50 refs.]

The only effective anti-tuberculous vaccines at present are those containing living organisms such as BCG or the vole bacillus. The possibility that organisms that have been attenuated artificially may regain their virulence has stimulated research into the immunizing power of fractions of the tubercle bacillus, and this paper presents the results obtained by the authors in experimental work.

Vaccines containing tuberculoproteins, polysaccharides and lipids were used and compared with BCG and vole bacillus vaccines in regard to their power to protect vaccinated guineapigs against the effects of superinfection with virulent tubercle bacilli (H37Rv).

The methods used to prepare these "synthetic" vaccines are described in detail. Different dosages were used as tabulated, and each animal received 6 injections of vaccine at intervals of 7 days, 2 intracutaneous, 2 subcutaneous and 2 intramuscular. Post-vaccinal tuberculin sensitivity was measured by the Mantoux test and thereafter the vaccinated and the unvaccinated control animals were superinfected.

The degree of tuberculosis present at death or when the animal was killed for autopsy was assessed by the state of the organs and the extent of the tuberculous lesions found. It ranged from moderate hypertrophy of an organ (1) to advanced generalized tuberculosis (16).

Vaccines containing tuberculoproteins, polysaccharides and lipids were ineffective and animals vaccinated with them survived for even shorter periods than unvaccinated controls.

In a series of 400 guineapigs 100 were vaccinated with a vaccine containing only tuberculolipids and saccharides, 100 with BCG, 100 with vole bacillus vaccine and 100 left as unvaccinated controls. An epizootic of pasteurella infection killed more than one-half the animals but the following results were obtained in the survivors:—

		180 days after superinfection			
	Alive and infected with H37Rv	Dead	Index of Disease	Killed	Index of Disease
Synthetic vaccine	47	43	7·5–16·0	4	5·5–8·5
BCG	26	22	7·0–14·0	4	7·0–12·0
Vole bacillus	46	36	4·0–11·5	10	7·0–11·0
Controls	47	46	11·0–16·0	1	15·0

It was concluded from the above that animals treated with this form of synthetic vaccine acquired considerable resistance to virulent superinfection. It was however less than that produced by the living vaccines.

H. G. Calwell

DEBRÉ, R. Les critères d'activité du vaccin B.C.G. [**The Problem of Standardizing BCG Vaccine**] *Bruxelles-Méd.* 1958, Dec. 14, v. 38, No. 50, 2069–91.

Chemical studies have shown only infinitesimal differences between BCG and virulent tubercle bacilli. The strain of tubercle bacillus known as BCG has attenuated virulence, and in culture it displays in some degree the cord formation which is characteristic of most virulent mycobacteria but which is not displayed by avirulent strains. BCG lies somewhere between avirulent and fully virulent strains, and although it does not multiply very actively in experimental animals it does not behave as a truly avirulent organism.

The development of the primary vaccinal complex in man is described. Post-vaccinal tuberculin conversion is the rule but in a very small proportion of vaccinated persons the Mantoux reaction remains negative.

Some persons are incapable of acquiring tuberculin sensitivity or at least of manifesting it by a positive Mantoux reaction but it must be remembered that a child vaccinated with BCG several times without displaying tuberculin sensitivity may convert after natural infection. Tuberculin sensitivity may not develop because of insufficient multiplication of the bacilli, and it may be that the factors which permit multiplication vary in different individuals or in the same individual at different times.

BCG may cause diffuse minimal lesions in vaccinated persons, as reported, for example, by SÉNÉCAL [this *Bulletin*, 1958, v. 33, 32] who found follicular lesions in specimens of liver removed by puncture.

Hyperglobulinaemia has sometimes been found after vaccination, and it is known that antibodies to antigenic extracts of the tubercle bacillus develop even before tuberculin conversion has occurred. The Middlebrook-Dubos reaction has been found positive in vaccinated persons even in the absence of tuberculin sensitivity.

The protective power of BCG seems to be largely dependent on its multiplication in the body, by which antigen is elaborated and new antigens are produced which are not found in cultures but only in the body of the host.

There exist many mycobacteria of attenuated virulence including those which have acquired resistance to isoniazid, and there are no certain means of identifying an organism as BCG. Workers in France and Japan have succeeded by repeated passage on bile medium in conferring the characteristics of BCG on other virulent human and bovine strains of the tubercle bacillus.

The many strains of BCG throughout the world, all derived from the original, do not possess the same degree of residual virulence, and it is certain that they are not and never were composed of a homogeneous bacillary population. Other factors which make for lack of uniformity are the age of the culture and the method of preparation, *e.g.*, whether fresh liquid or freeze-dried vaccine is made.

Methods used to assess the activity of the vaccine include bacillary counts, observing multiplication in cultures or animals by means of radio-active isotopes, observing the course of the vaccination lesion and the development of tuberculin sensitivity and finally large-scale follow-up of vaccinated persons as in the British Medical Research Council's trial [this *Bulletin,* 1956, v. 31, 621].

The activity of a BCG vaccine can only be assessed by correlating all the data emerging from observations such as these. To do so requires full cooperation between those who produce and those who use the vaccine. *H. G. Calwell*

KERR, Mary R. & DUNBAR, J. M. **Tuberculous Meningitis following B.C.G. Vaccination.** *Brit. Med. J.* 1958, Oct. 25, 1019–20.

An infant aged 2 months living in a caravan in Scotland with her mother, father and brother was tested with tuberculin and did not react. The date of this test is not given. On June 29, 1956, she was vaccinated with BCG [dose or kind of vaccine not stated], and 8 weeks later she was found to be a reactor (Mantoux 10 TU of OT).

On April 1, 1957, over 9 months after vaccination, she was admitted to hospital with tuberculous meningitis, having been ill 8 days. Details of the clinical and laboratory findings are given. The infecting organism was shown to be a virulent strain of *Mycobacterium tuberculosis* of the human variety. [BCG is a bovine strain.] Treatment with streptomycin, isoniazid and PAS was given with complete success.

The medical history of the family is related. The mother had had sputum-positive pulmonary tuberculosis in 1952. Her state at the material time is not described. The father had pulmonary tuberculosis which was believed to be inactive although he was still being examined by X-ray every 3 months. [Such frequent observation is hardly consistent with an opinion of inactivity of the disease.] The brother, aged 19 years, had a lung cavity in 1956 but tubercle bacilli were never found. The appearance of the lesion was improving with chemotherapy.

[Here then was an infant living in a single apartment in a markedly tuberculous environment. There is no evidence that she was isolated from it at birth and vaccinated with BCG in isolation, but she was vaccinated on a single tuberculin test at the age of 2 months. It is remarkable that this could happen in the United Kingdom at the present time except through the recalcitrance of parents. It is axiomatic that, wherever possible, contact between an infant and a person with infectious or potentially infectious tuberculosis should be broken at the earliest possible moment and for 6–8 weeks before and 6–8 weeks after BCG vaccination if vaccination is advised. The infant in this case appears to have been exposed to 1 or more infectors from birth, and her illness could have occurred at any time from the age of 4–5 months. It is the method of control used here rather than the failure of BCG to protect that the reviewer considers should be publicized.] *H. G. Calwell*

KERR, Mary & DUNBAR, J. M. **Tuberculous Meningitis after B.C.G.** [Correspondence.] *Brit. Med. J.* 1959, Jan. 10, 114–15.

In the original paper [above] it was stated that the mother had had sputum-positive pulmonary tuberculosis in 1952, that the father had a pulmonary lesion believed to be inactive and he was being X-rayed every 3 months and that the brother had a lung cavity but tubercle bacilli had never been recovered and he was receiving chemotherapy with benefit.

The report of the case in the above terms and with such scanty details aroused such interest that the authors gave a more detailed account of the epidemiology. It was now reported that the mother's disease was completely arrested at the time of the birth and afterwards, that the brother never had cavitation but had a calcified primary complex and that the father was a healthy man who had had 1 previous X-ray examination as a contact, which was negative.

In February 1957 (about 1 month before the child's health began to fail) the brother was X-rayed as a national service recruit and found to have active pulmonary tuberculosis. Tubercle bacilli were found on culture. In the same month a small pulmonary lesion of doubtful activity was found in the father; this was proved to be inactive. [No information is given about the date of his previous contact X-ray examination when no lesion had been seen so that it is not certain when the new lesion appeared.] In the authors' opinion the infant was infected by her brother about February 1957.

[This failure of BCG vaccination to protect the child is of great interest. The development of tuberculous meningitis in successfully vaccinated children is rare. According to WALLGREN'S time-table tuberculous meningitis after primary infection usually occurs 3 months

after the appearance of tuberculin sensitivity, *i.e.*, some 4–5 months after infection. In the case reported infection could have occurred much earlier in the child's life than the 8th or 9th months, and within 3 months of vaccination. As the brother was not X-rayed from March 1956 to February 1957 it is not known when his disease became active but on the evidence presented it is probable that he was infectious long before February 1957. The case appears to show that BCG vaccination may fail to prevent disease when infection occurs early in the post-vaccinal period.] *H. G. Calwell*

VENEREAL DISEASES

POULSON, N. H. **The Clinical Interpretation of Serological Reactions in Venereal and Endemic Treponematosis.** *Amer. J. Pub. Health.* 1958, Dec., v. 48, No. 12, 1622–7. [10 refs.]

The differential diagnosis between syphilis and endemic treponematosis [which in this case is yaws] is often difficult and especially so in Guamanians who represent most of the patients in this communication; the classical serum tests for syphilis, and even the TPI test, do not distinguish between the two.

Yaws is common in Guam and syphilis rare among the indigenous population but there is a transient military population in the islands which complicates the issue; in addition, most cases of yaws can be cured by a single injection of repository penicillin [yet the author employed 5 or more injections], but syphilis requires more intensive treatment.

Of 10,855 blood specimens tested by means of the Kahn, Mazzini or VDRL tests, or a combination of these, 839 (7·7%) were positive. 310 persons who gave positive reactions were investigated, most of whom were in the 10–20 or 21–40 age-groups; differential diagnosis depended on history, scars of old chancres or healed yaws (nursing-type or tissue-paper scars) and reaction to previous treatment.

The 310 patients were divided into 2 groups:

Group I (103 patients) were undetermined cases demanding further treatment and observation; only 2 had active yaws and these were treated with 3 mega units of penicillin; others received up to 9 mega units; 8 were rechecked and of these 5 remained positive and 3 became negative.

Group II (207 patients) included 97 who had had adequate treatment previously and 110 who had presumably not been treated.

4 typical case histories are given in some detail: one patient had received 5 injections each of *0·6 "grams"* of mapharsen [it is surprising that this patient survived such drastic treatment].

It is concluded that serum reactions may remain positive in cases of treated yaws for long periods, that yaws protects against syphilis and that each case must be examined critically to avoid unnecessary treatment which may cause severe social and economic damage.

T. E. Osmond

RAJAM, R. V. **Inter-Laboratory Evaluation of Serological Tests for Syphilis in India. Final Report on 1953–55 Inquiry.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 6, 995–1040.

This long article of 45 pages contains a vast amount of detail including 14 tables and is unlikely to be studied by anyone except the serologist.

Essentially it reports the results of parallel tests carried out in 8 different laboratories on 921 sera employing the Wassermann (WR) and Kahn tests (with crude antigen) and the VDRL test (with cardiolipin antigen).

The sera included 376 from syphilitic persons, 86 from persons with venereal diseases other than syphilis, 265 from persons with other diseases and 194 from apparently normal persons. The qualities of each test particularly studied were specificity, sensitivity and reproducibility. The average percentages of 6 laboratories were:—

WR: specificity 86, sensitivity 86 and reproducibility 77; the corresponding figures for the Kahn were 98, 83 and 83 and for the VDRL 98, 95 and 87.

Thus it will be seen that the VDRL proved superior to the other tests and it is recommended that this test be adopted for routine use in all laboratories.

The standards of the various participating laboratories varied considerably—from good to only fair; most need improvement and for this purpose standardized reagents are advised together with annual serological surveys. Tests should be quantitative as well as qualitative.

All tests gave some biological false positive reactions and for this reason a reference laboratory should be set up where, in addition, the TPI test could be carried out.

T. E. Osmond

BUBE, F. W. Sieben Luesreaktionen im Vergleich. **[Comparison of Seven Serological Syphilis Tests]** *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 5/6, 479–85, 2 figs. [28 refs.]

Complement-fixation tests with 4 antigens and 3 flocculation tests were carried out on sera from 1,343 cases of verified syphilis, slight and doubtful sera being excluded from the investigation. The antigens used in the complement-fixation test were heart extract, syphilitic liver extract, pallida antigen and cardiolipin. The flocculation tests were the Meinicke II, Citochol and VDRL. Of these the greatest sensitivity was shown by the VDRL which gave 97·4 positive results. Complement-fixation with pallida antigen gave the best complement-fixation reaction results but this does not represent the real sensitivity as 300 of the 322 negative sera gave positive results when relatively larger quantities of serum were used. In some instances only the VDRL and the pallida complement-fixation test gave positive results. The authors conclude that both these tests should be employed in any serological investigation of syphilis.

P. A. Clearkin

SINNECKER, H. Zur Prüfung von Luesextrakten und Antigenen auf antigene Wirksamkeit und Unspezifität. [**The Determination of the Antigenicity and Unspecificity of Antigens for Serological Syphilis Reactions**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, Nov.–Dec., v. 116, Nos. 5/6, 439–52, 4 figs.

Developments in the serology of syphilis during the last decade, especially the introduction and increasing use of quantitative tests after the development of cardiolipin antigen and of standard procedures with the help of standardized syphilitic sera, have rendered it necessary to re-examine the State regulations for control of syphilitic antigens.

State control of syphilis antigens in Germany was introduced in 1934 by a decree of the Ministry of the Interior. This decree ordered that an antigen should be tested in comparison with 2 others and that tests should be carried out with 24 positive sera, 30 negative sera and 10 sera which tended to give a biological false positive result. The permissible limits of deviation of an antigen for the qualitative test were laid down.

The author of this paper carried out a series of investigations to determine the value of the prescribed tests and concludes that the regulations for testing the antigen for qualitative tests were satisfactory but that the definition of the tolerated deviation should be altered to plus or minus 20% of the relative amount of positive results. Preparations for quantitative reactions should be tested by quantitative methods and the tolerated deviation should be plus or minus 20% of the sensitivity. If 1 out of 40 sera gives an unspecific reaction 60 more sera should be used; if 2 out of 40 give an unspecific reaction 110 more sera should be used and their specificity determined within the limits of the tolerated deviation. *P. A. Clearkin*

WARING, G. W., Jr., LANES, A. S. & MESCON, H. **Biological False-Positive Results in Serologic Tests for Syphilis. Findings in a Low Socioeconomic Population Group.** *J. Amer. Med. Ass.* 1958, Dec. 13, v. 168, No. 15, 2004–5.

The circumstances of 75 patients who gave persistent positive classical serum reactions for syphilis were investigated; no patient gave any history or showed any signs of syphilis. 23 were Caucasians with a widely varying socio-economic background; in 39% of these the TPI test was negative; the other 52 patients were Negroid forming a [?low] homogeneous socio-economic group; all of these gave positive TPI reactions.

The conclusion drawn by the authors is that false positive serum tests for syphilis are much more common in the high than in the low socio-economic classes; they stress the necessity of epidemiological investigations in the diagnosis of syphilis and point out that laboratory tests in themselves are not diagnostic.

T. E. Osmond

DULAC, E. P. Les antigènes tréponémiques dans le diagnostic des tréponématoses exotiques. [**Treponemal Antigens in the Diagnosis of Treponematoses in the Tropics**] *Méd Trop.* Marseilles. 1958, Sept.–Oct., v. 18, No. 5, 783–92.

(2940)

Infections caused by treponemata occupy an important place in the endemic diseases of Tropical Africa, yaws and bejel in the country districts, venereal syphilis in towns. Diagnosis therefore presents a problem to the physician. The cost and complexity of the Nelson test have militated against its use in the tropics. The test required in tropical regions is a reaction with the simplicity of the cardiolipin test and the reliability of the treponema immobilization test of Nelson.

The author submits results of 3,000 serological tests carried out in the Upper Volta and Mauritania districts of French West Africa and compares his results with those obtained in Europe. The tests employed were the flocculation reaction of Kline, the VDRL and the complement-fixation test of Kolmer compared with a complement-fixation test in which the Pallignost technique with a treponema extract as antigen was used. The results showed that the treponema antigen suspension was sensitive, specificity was good but its stability was uncertain and the reactions could not always be reproduced. The sensitivity of treponemata extracts was weak and gave abnormal reaction with old or altered sera. The Meinicke test gives erratic results in hot climates, the Kahn is "fertile in surprises" and is liable to give false positive results and show zone phenomena. Even the VDRL was found to vary but the Kline checked by a quantitative reaction appears to be satisfactory. The author concludes that the best reaction for African conditions is the Kolmer and the Kline qualitative and quantitative with heated sera and cardiolipin antigen. Addition of other reactions does not facilitate interpretation of discordant or varying serological results in the case of old or latent treponema infections. *P. A. Clearkin*

ROEMER, G. B. & SCHLIPKÖTER, H. W. Die Spirochätenagglutination im Serum, ein Beitrag zur Serodiagnose der Lues. [**Spirochaete Agglutination in the Serodiagnosis of Syphilis**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 422–38. [37 refs.]

In this long paper the authors discuss the characters of the diagnostic tests for syphilis in which use is made of spirochaetes obtained from syphilitic orchitic tissue. In these tests either living organisms as in the Nelson immobilization test or dead organisms or extracts from them are employed in other procedures which have been developed. Among the drawbacks of these tests are their complexity and cost which preclude their introduction as routine procedures. Simpler than these methods are some which are based on the use of spirochaetes cultured in the laboratory such as the Reiter strain. There is an account of some of the published work on the lipoid and protein antigens in this strain.

In 1948 Roemer reported on the use of the Reiter strain in an agglutination test for antibodies in cerebrospinal fluid in suspected cases of syphilis of the nervous system [this *Bulletin*, 1949, v. 24, 319]. Later in 1955 both authors of the present paper published results with the test adapted for use in serodiagnosis in 1,250 sera [*ibid.*, 1955, v. 30, 589]. Some modifications of the test have now been made and are described. The results of its use in the examination of about 12,000 sera are

reported at considerable length. Of these sera 161 were from patients with proved syphilis, most of whom had been treated, and a positive agglutination test was obtained in 82%. In early syphilis positives were 100%. These findings were compared with those obtained by various routine tests. An advantage of the method is its simplicity and it is considered to be suitable for the routine quantitative determination of spirochaetal agglutinins in syphilitic sera. *M. E. Delafield*

BURGESS, J. A. **Syphilitic Foetus after Prenatal Penicillin Therapy.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 240.

"A case is described in which a pregnant woman received a course of penicillin injections, and was delivered 4 weeks later of a syphilitic foetus.

"It is suggested that anti-syphilitic treatment should be given immediately to expectant mothers in whom the initial serological tests for syphilis are unequivocally positive."

RAJAM, R. V. & RANGIAH, P. N. **Spontaneous Cure of a Popliteal Aneurysm of Syphilitic Aetiology.** *Brit. J. Venereal Dis.* 1958, Dec., v. 34, No. 4, 210–12, 1 fig.

KLIENEBERGER-NOBEL, E. **Pleuropneumonia-Like Organisms in Genital Infections.** *Brit. Med. J.* 1959, Jan. 3, 19–23. [14 refs.]

This article reports the results of an investigation into the incidence of pleuropneumonia-like organisms (PPLO) in genital infections and controls. Cultural methods were found to be the most reliable and centrifuged urine the most satisfactory source. The medium employed contained boiled blood, heart infusion, peptone agar with "oxoid" yeast extract, deoxyribonucleic acid, pooled human serum, thallium acetate, penicillin and staphylococcus broth culture filtrate [for details the original should be consulted].

98 strains were isolated and their characteristics are described; of 48 tested all were resistant to penicillin, sulphonamides, erythromycin and oleandomycin but more or less sensitive to the tetracycline group, streptomycin, chloramphenicol, spiramycin and neomycin.

Of the control group of males only 3% of 100 men showed PPLO and of 47 boys under 14 none were positive. Among male VD patients 48% of those with recent non-gonococcal urethritis (NGU), 30% of those with untreated gonorrhoea, 10% of those with Reiter's disease, but none of those with chronic NGU were positive.

Of 59 women attending a VD department 56% showed PPLO and of 109 obstetric or gynaecologic patients 20% were positive.

Of 7 pairs of consorts, in 4 where the male had recent NGU or gonorrhoea both showed PPLO; in the other 3 both partners were negative.

Thus it appears that PPLO are commonly found in males with recent NGU or gonorrhoea but are rarely found in healthy male adults or boys; other observers have found PPLO far more frequently in apparently healthy males; these organisms are found more frequently in women than in men; they do not appear to be common in Reiter's disease.

The author considers that these organisms are probably pathogenic. *T. E. Osmond*

OTHER COMMUNICABLE DISEASES

The order of papers in this section is as follows: Tetanus; other diseases.

DAMANY, S. J. & KAMAT, G. R. **Meprobamate in Tetanus.** *J. Indian Med. Ass.* 1958, Nov. 16, v. 31, No. 10, 394–7.

Standard treatment for tetanus in the Vadilal Sarabhai General Hospital, Ahmedabad, India consisted of antitoxin, adequate nutrition, penicillin and sedation with paraldehyde and phenobarbitone. This treatment was given to 1 group of 27 patients: to a second group of 39 patients meprobamate was given in addition, the dose for an adult being 800 mgm. every 6 hours. The mortality in the second group was 23·1% compared with 29·5% in the control group, a difference which the authors agree was not significant. They felt that meprobamate might have had some beneficial effect on the milder cases. Side effects were few and minor.
A. B. Christie

BOGGS, D. R., FREI, E. & THOMAS, L. B. **Clostridial Gas Gangrene and Septicemia in Four Patients with Leukemia.** *New England J. of Med.* 1958, Dec. 25, v. 259, No. 26, 1255–8, 2 figs. [12 refs.]

This report includes clinical and pathological details of 4 instances in which clostridial septicaemia occurred in association with leukaemia. The site of clostridial infection was probably the mucosa of the gastrointestinal tract where there was extensive leukaemic infiltration and necrosis. In 1 of the patients, diagnosis was made during life by blood culture and the septicaemic condition responded to treatment with 20 million units of penicillin and 2 gm. of streptomycin daily along with blood transfusion, cortisone and oxygen.
A. B. Christie

VAN GELDEREN, H. H. & DE MAN, J. C. H. **Cytomegalia infantum.** *Nederl. Tijdschr. v. Geneesk.* 1959, Jan. 31, v. 103, No. 5, 211–16, 3 figs. [23 refs.]

The English summary appended to the paper is as follows:—

"Description of a case of congenital generalized cytomegalia infantum (salivary gland virus disease). The diagnosis was made shortly after birth on the typical clinical picture of erythroblastosis, thrombocytopenia, icterus and hepatosplenomegaly without blood group incompatibility, and confirmed by the giant cells found in biopsy material from parotis and liver. No giant cells were found in the urine. The child recovered following prednisone therapy. At the time of writing (ten months after birth) she is alive and healthy.

"This is the sixth case diagnosed in a living child and described in the literature, and the third case on record to survive.

"Infection with the virus of cytomegalia often leads to formation of giant cells in the salivary glands, and less often in other organs.

"As far as is hitherto known, distinct and typical symptoms are found only in the congenital generalized form.

"An early diagnosis is essential, as recovery may be effected by cortisone therapy. Without treatment death is often inevitable."

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order: General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; others.

For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

TASSELLI, E. Diffusione, epidemiologia e profilassi della brucellosi umana in provincia de Matera. [**Propagation, Epidemiology and Prophylaxis of Human Brucellosis in the Province of Matera**] *Ann. d. San. Pubblica.* Rome. 1958, Sept.–Oct., v. 19, No. 5, 1065–88, 3 graphs & 1 map. [20 refs.] English summary.

Matera is one of the 2 provinces of the Basilicata region of southern Italy and has a population of nearly 200,000, most of whom at present live in aggregations though their work is almost entirely agricultural (see below). The author, who is the State Veterinary Officer, gives a table showing *Brucella* notifications for the whole country from 1930–57. Matera has a high incidence, most of the infections being in males. The incidence is highest in the 21–30 age-group for both sexes, with the 11–20 group next. The disease is more frequent in the warmer months reaching a peak in May.

Br. abortus is almost absent and cattle do not represent a serious source of infection, which is due to *Br. melitensis* transmitted by sheep and especially goats. Tasselli points out that in goats there may be no symptoms and that many families in the urbanized areas keep one or two for milking. Sheep on the other hand are raised in flocks away from the inhabited areas, though they are a danger because of their passage between the plains and the mountains according to season, but unlike goats their milk is usually made into cheese and not used at once.

In one-half the human cases neither milk nor its derivatives could be blamed but all the patients had been in contact with infected goats; 16% more had had no contact with goats and had presumably been infected through eating contaminated raw vegetables, while in 3% direct human contact was suspected. In the rural areas the so-called "field-salad" which grows along ditches and small streams contaminated by feeding animals is also thought to be important.

Prevention: the main attack was on the goats, since campaigns against sheep are difficult and uneconomic though efforts are being made to eliminate infected rams. Starting in 1956 in the 9 communes in the province with the highest human incidence, compulsory testing by brucellin and slaughter of reactors began, the owners being compensated. Reactors which could not be eliminated were sequestrated and indelibly stamped. The results showed that of 28,065 tested, 1,383 (4·92%) were positive and 1,306 were slaughtered, and in the first 4 months of 1958 only 17 human cases were notified—the lowest figure for at least 13 years. Tasselli concludes that the high incidence is due mostly to the number of goats living in the inhabited areas and to the grave sanitary deficiencies existing there, but that if the isolation and slaughter policy is extended to the whole province this is likely to prove an effective prophylactic measure.

[The author mentions that recent land reforms have given what are to all intents and purposes smallholdings, to a number of agricultural workers, so presumably the concentration of people and goats has lessened in the denser areas, but the relatively stable goats are more easily dealt with than the peripatetic sheep flocks. The importance attached to infection through eating contaminated raw vegetables is interesting.]

W. K. Dunscombe

LINSERT, H. Serodiagnostische Untersuchungen auf Brucellose bei Tierärzten unter Berücksichtigung der Flockungsreaktion. [**Brucellosis in Veterinary Surgeons. Serological Examinations including Flocculation Tests**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 3/4, 232–7. [12 refs.]

Veterinary surgeons run a risk of contracting brucellosis owing to their occupation and the author examined 104 of them, using agglutination, flocculation and complement-fixation reactions in order to determine the extent of the risk. Of the 104 tested, 51 (49·03%) were positive to *Brucella abortus*, 10 (9·62%) were doubtfully positive and 43 (41·35%) were negative. It was found that all 3 tests were required. Slow agglutination alone is not sufficient to determine the antibody levels.

P. A. Clearkin

PARNAS, J. Untersuchungen über diagnostische Allergene bei der Brucellose, der Tularämie, dem Malleus und dem Rotlauf. [**Examinations on Diagnostic Allergens in Brucellosis, Tularaemia, Glanders and Erysipeloid**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1957, v. 114, Nos. 2/3, 186–205, 8 figs.

This communication discusses in much detail the methods of preparation and the results obtained with diagnostic allergens in the conditions of brucellosis, tularaemia, glanders and erysipeloid. It is maintained further in the case of brucellosis that the preparation used, Brucellin PD, is more valuable than the antibiotics in the treatment of chronic infection if repeated injections are administered.

Brucellin. For the preparation of this material a heavy suspension from a 3–4-day culture on glucose horse serum agar is subjected to ultrasonic disintegration.

Tularin. The preparation used for diagnosis of tularaemia described as Tularin U is obtained from growth of an immunogenic but non-pathogenic strain on the medium of McCoy-Chapin and in this case also the suspension is disintegrated by ultrasonic vibration, the result being controlled by the ultramicroscope. This reagent is valuable in giving positive reactions even in the early phases of the disease and the results coincide well with the clinical history and with other immunological reactions.

Mallein. In preparing mallein for the diagnosis of glanders, it has been found of advantage to replace the older preparation made from glycerin broth by a suspension from solid culture disintegrated by repeated freezing and thawing, described as Mallein PS.

Rhusiopathin. In the case of *Erysipelothrix*, the washed sediment from cultures is disintegrated by incubation in N/10 NaOH solution. This preparation is described as Rhusiopathin L. An extensive record of experimental findings is given which includes a number of non-specific results; but examples are given of clinical observations demonstrating the value of the preparation. *J. W. McLeod*

Austoni, M., Bertelli, G. & Babudieri, B. Anticorpi antileptospira e frazioni proteiche del siero. [**Antileptospiral Antibodies and the Protein Fractions of Antisera**] *Giorn. di Malattie Infettive e Parassit.* 1958, June, v. 10, No. 6, 488–91.

Experiments were carried out to determine with which protein fractions of antiserum leptospiral antibodies are associated. The fractions, separated by electrophoresis, were tested for the presence of agglutinins in the usual manner.

A preliminary experiment was made with sera obtained respectively from one patient recently recovered from Weil's disease, from one patient 8 years after recovery and from a guineapig which had survived infection with a strain of *Leptospira icterohaemorrhagiae* of low virulence. In all cases the antibodies were associated only with the γ-globulin fraction but the agglutinin titres were notably lower than those of the whole serum. There were also differences among the 3 sera: in the recently recovered case the antibodies were entirely in the γ2 fraction; in the guineapig they were mainly in the γ2 fraction but were present also in γ1; in the old case all the agglutinins were in the γ1 fraction.

A further series of tests were made on 15 sera from people with Weil's disease—6 taken in the active stage of illness or during convalescence, and 9 collected at various intervals from 5–19 years after recovery. The predominant association of antibody in sera from old and recent cases with the γ1 and γ2 globulin fractions respectively was apparent in this series also, but in only a few cases were the antibodies limited entirely to one fraction. Nevertheless, the authors consider that there is undoubtedly a tendency for this change to occur.

J. C. Broom

Langham, R. F., Morse, E. V. & Morter, R. L. **Pathology of Experimental Ovine Leptospirosis, *Leptospira pomona* Infection.** *J. Infect. Dis.* 1958, Nov.–Dec., 285–90, 9 figs. [17 refs.]

Graber, R. E. & Pomeroy, B. S. **Ornithosis (Psittacosis): an Epidemiological Study of a Wisconsin Human Outbreak transmitted from Turkeys.** *Amer. J. Pub. Health.* 1958, Nov., v. 48, No. 11, Pt. 1, 1469–83, 1 fig. [13 refs.]

This paper reports the findings of 2 epidemiological studies, on psittacosis in turkey flocks in Wisconsin and on infection with this agent in human beings exposed to turkeys. Both surveys extended over 2 years; the one on turkeys began a little over a year before the other. 124 turkey flocks were surveyed. There was little or no clinical evidence of infection in the birds, though by means of the indirect CFT it was shown that approximately one-half the flocks were infected. The few strains of psittacosis virus isolated were of low virulence for mice. The human population surveyed was the staff of 248 persons in a turkey processing plant receiving birds from Wisconsin and East Minnesota farms.

According to serological, together with epidemiological and clinical, evidence 19 cases of infection with psittacosis virus occurred in the 2-year period, of which 9 were inapparent. All the other 10 patients recovered.

S. P. Bedson

Jannach, J. R. **Myocarditis in Infancy with Inclusions Characteristic of Psittacosis.** *J. Dis. Children.* Chicago. 1958, Dec., v. 96, No. 6, 734–40, 8 figs. [15 refs.]

This is a description of a rapidly fatal case of myocarditis in an 18-month-old child. The evidence that it was due to psittacosis virus was the finding of typical virus-containing cells in sections of myocardium and the isolation of psittacosis virus from 2 budgerigars with which the child had been closely associated.

S. P. Bedson

Diseases due to Fungi

For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

GRIN, E. I., ZEC, N. & ŠTERN, P. Trihofitija kapilicija odraslih i hormonalna disfuncija oboljelih. [**Hormonal Dysfunction in Adults infected with Ringworm of the Scalp due to** *Trichophyton*] *Naučno Društvo NR Bosne i Hercegovine.* Sarajevo. Sect. Med. Sci. IX. 1958, No. 5, 5–14, 5 figs. on 3 pls. [14 refs.] English summary.

Ringworm of the scalp due to *Trichophyton violaceum* was found in 795 of 10,534 persons examined in the district of Breko, Yugoslavia. The incidence was relatively high before puberty in both males and females, but in adults the infection was found mainly in females, and in a group of these the excretion of 17-ketosteroids in the urine was found to be below normal values. Many of the (comparatively few) infected male adults showed somatic changes characteristic of dysfunction of the endocrine glands, tending towards a female pattern.

The authors think that some disturbance of the endocrine-neurovegetative system may be a factor in this infection, probably disturbed adrenocortical function, though proof is lacking. *Charles Wilcocks*

MANSON-BAHR, P. E. C. **Histoplasmosis in East Africa.** *East African Med. J.* 1958, Nov., v. 35, No. 11, 625–9. [13 refs.]

After a general review of the disease the author recalls 2 examples of infection by *Histoplasma capsulatum* previously recognized in East Africa. The first, seen in Nairobi, was a European male whose disease appeared to be limited to a granuloma of the vocal cords, which was removed. The pathogenic yeast phase of the fungus was demonstrated in the specimen and a positive histoplasmin skin test at an antigen dilution of 1/100 was obtained. Recovery was complete. The second described by DAVIES [this *Bulletin*, 1958, v. 33, 234] from Machakos was an example of systemic histoplasmosis in a European child aged 2½ years which proved fatal after an illness lasting 6 months.

The author then describes 2 new examples of the disease in an Englishman and his wife, who had explored a set of bat-infested caves at Amboni near Tanga, in the valley of the Siti River in Tanganyika. After an interval of 14 days the male patient developed a high sustained fever with heavy sweats and a harsh dry cough. The general condition remained remarkably good, no anaemia developed and the leucocyte count did not rise above 10,000 per cmm. No pathogens could be isolated from the tenacious, mucoid sputum. X-ray examination showed ill-defined, coarse mottlings, 3–5 mm. in diameter, scattered throughout both lungs. Some 2 months from the onset the histoplasmin skin test gave a strongly positive reaction at a dilution of 1/1000, and the histoplasmin CFT in the plasma was positive to a titre of 1/64.

Fever subsided slowly over a period of 2 months, apparently being uninfluenced by penicillin, chloramphenicol, nystatin, sulphonamides, 2-hydroxystilbamidine to a total dosage of 2·5 gm. and large doses of potassium iodide. 5 months later abnormal radiological signs were still evident in the lungs.

The patient's wife developed a transient fever without cough but was free from radiological changes in the lungs. She developed a positive histoplasmin skin test but the CFT remained negative.

The author points out that the growth of a saprophytic form of the fungus is particularly favoured by soil fertilized by animal droppings, such as is to be found in many caves, and suspects that the human disease is widespread in East [*ibid.*, 1954, v. 29, 367] and South Africa [*ibid.*, 1957, v. 32, 664] where histoplasmin skin test surveys have already shown positive incidences of 8·5 to 14·6%, the latter in African gold miners from Nyanza province. *J. H. Walters*

MILLER, J. M., GINSBERG, M., JOHNSON, H. R. & BOGOSIAN, A. **The Treatment of Histoplasmosis with Amphotericin B (Fungizone).** *Antibiotic Med.* New York. 1958, Oct., v. 5, No. 10, 593–7, 6 figs.

An ulcerated swelling of the lower lip in a man of 71 was diagnosed as an epithelioma and excised: histology changed the diagnosis to histoplasmosis. Further lesions appeared on the tongue and soft palate in which *Histoplasma capsulatum* was demonstrated. Treatment with 225 mgm. 2-hydroxystilbamidine daily for 23 days was ineffective. Treatment with amphotericin B given intravenously in a dose of 10 rising to 40 mgm. daily for 28 days cured the condition and caused no ill effects. 1 gm. acetylsalicylic acid was also given 3 hours before, at the time of, and 3 hours after, the dose of amphotericin, and this is believed to have prevented the "shaking chills and fever" which this drug may otherwise produce. *L. P. Garrod*

DI EGIDIO, M. Micosi scroto-peniena da "*Candida (Monilia) albicans*". [**Mycosis of Scrotum and Penis due to** *Candida albicans*] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1958, Nov., v. 39, No. 11, 677–84, 5 figs. [11 refs.]

The English summary appended to the paper is as follows:—

"The author reports a case of chronic moniliasis (Candida albicans) localized in scrotum and penis, successfully treated by local administration of Hg Cl_2 1/1000 and applications of U.V. rayons."

WILSON, L. L. **Cryptococcosis (Torulosis): a Report of Nine Cases.** *Australasian Ann. of Med.* 1958, Nov., v. 7, No. 4, 276–85, 6 figs. [39 refs.]

"Five cases of cryptococcosis occurred in South Australia during 1957. Only four other cases (also described here) were recognized in the previous ten years. In four cases in this series the patient had a preceding respiratory infection followed by pulmonary cryptococcosis, and three of these developed central nervous system involvement. Isolated pulmonary lesions, cerebral granuloma and spinal cord involvement are rare forms of cryptococcosis which also occurred in this series.

"No treatment has proved effective; 'Amphotericin B' and 'Fungizone', now under trial, were unsuccessful in two cases here. Surgical removal of isolated brain and lung lesions may help, but earlier diagnosis, perhaps by the development of immunological tests, is highly desirable. Because of its varied manifestations, cryptococcal meningitis is difficult to diagnose until late in the course of the disease.

"The cause of human infection is unknown, but it must be related in some way to the resistance of the host, as well as to variations in virulence or type of the fungus. The significance of contact with pigeons is discussed."

BREDE, H. D. Zur Aetiologie und Mikrobiologie der Aktinomykose. I. *In-vitro*-Versuche zur Frage der fermentativen Unterstützung des *Actinomyces israeli* durch Begleitbakterien. [**The Aetiology and Microbiology of Actinomycosis. I.** *In vitro* **Test on Fermentative Support of** *Actinomyces israeli* **by Bacterial Symbionts**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 1/2, 110–22. [16 refs.]

HEINRICH, S. & PULVERER, G. II. Definition und praktische Diagnostik des *Actinobacillus actinomycetem-comitans.* [**II. The Definition and Practical Determination of** *Actinobacillus actinomycetem-comitans*] *Ibid.*, 123–35, 10 figs. on 2 pls. [21 refs.]

The English summary appended to the paper is as follows:—

"Previous investigations have realised that most probably all cases of human actinomycosis show a mixed bacterial flora. The etiological rôle of the symbionts by fermentative support of Actinomyces israeli seems to be beyond any doubt. The production of depolymeridases by Actinomyces israeli on the one hand and by the symbionts on the other hand was investigated, using viscosimetric and decapsulation tests.

"The following results were obtained:

"1. The filtrates of cultures of 88 Actinomyces strains did not contain depolymerizing enzymes.

"2. Hyaluronidase was found in all 21 Staph. aureus strains, isolated from cases of actinomycosis. This substance acts as diffusion factor by depolymerization.

"3. In 22 of 25 filtrates of cultures of Actinobacillus actinomycetem comitans depolymeridases could be detected. Their action differed from that of hyaluronidase.

"4. All 21 Bacterioides melaninogenicus strains produced depolymeridases, but not hyaluronidase.

"5. 3 of 8 anaerobic streptococcus strains tested produced hyaluronidase."

"A survey of the literature shows that the Actinobacillus actinomycetem-comitans, which is frequently found as a symbiont of the Actinomyces israeli, is defined rather incompletely. Thus its differentiation and determination may present some difficulties.

"On the basis of many years of experience the morphological and cultural characters of A. c., including its cultivation on solid and liquid media, are described in detail. The characteristic colonial picture is illustrated by a series of micrograms.

"The results of the biochemical and serological examination of 12 comitans strains, isolated from human cases of actinomycosis are given. The strains tested proved to be biochemically and serologically uniform."

MANNING, L. K. & ROBERTSON, L. **A Case of Aspergillosis treated with Nystatin.** [Memoranda.] *Brit. Med. J.* 1959, Feb. 7, 345–6, 1 chart. [11 refs.]

A nurse, aged 36, was admitted to hospital with a chronic pyopneumothorax and bronchopleural fistula which had followed a lower lobe resection some years previously. *Aspergillus fumigatus* was isolated in pure culture from the sputum and from intrapleural pus, and it seemed probable that this organism had established itself as a result of treatment over 16 days with chlortetracycline previous to her admission.

500,000 units of nystatin suspended in 4 ml. of water were given by intrapleural instillations on successive and, later, alternate days to a total of 15·5 million units in 38 days. No side effects were noted, probably because nystatin was not absorbed into the blood stream. After one week of treatment the volume of sputum produced had fallen to half. Then, however, *Staphylococcus aureus* was also found to be present and chloramphenicol was given by intrapleural instillation in addition to the nystatin. With this treatment the temperature settled, the volume of sputum diminished and the patient improved. *A. fumigatus* was not isolated during the next 3 months.

It was noted that although *in vitro* resistance of the fungus to nystatin was demonstrated after only 2 or 3 sub-cultures, the patient was treated for 38 days without the emergence of a resistant strain. *Peter Abbott*

Rheumatic Diseases

CORNFELD, D., WERNER, G., WEAVER, Ruth, BELLOWS, Marjorie T. & HUBBARD, J. P. **Streptococcal Infection in a School Population: Preliminary Report.** *Ann. Intern. Med.* 1958, Dec., v. 49, No. 6, 1305–19, 4 figs. [17 refs.]

This article is critical of schemes for the prophylaxis of rheumatic fever by which penicillin treatment is given to school children in the mass merely on the evidence of a positive throat swab for haemolytic streptococci. The authors studied 1,000 children in 3 schools in Philadelphia during a period of 2 years. In school G, oral penicillin G 200,000 units 4 times daily for 10 days was given to all children with positive streptococcal throat swabs whether with symptoms or not; in school B the penicillin was given only to the children with symptoms as well as positive swabs; in school W no penicillin was given at all. It was found that: about one-half of the children had one or more positive cultures in the course of a year regardless of the attempts to control carriers with penicillin; that the percentage of children with symptoms of streptococcal disease was low in all 3 schools; and that a very small percentage of the children with respiratory symptoms had positive throat swabs for β haemolytic streptococci, and even those had symptoms mainly of the " febrile catarrh " type. In addition a large proportion of the group A strains isolated were untypable. The poured-plate method of culture yielded a higher recovery rate of streptococci than any enrichment or streaking method.

It is felt that in order to determine established streptococcal infection, serological methods for detection of antibodies are required in addition to culture of throat swabs. *H. Stanley Banks*

WERNER, G., CORNFELD, D., HUBBARD, J. P. & RAKE, G. **A Study of Streptococcal Infection in a School Population: Laboratory Methodology.** *Ann. Intern. Med.* 1958, Dec., v. 49, No. 6, 1320–31. [21 refs.]

The bacteriological methods used in the above study are here described. Comparative data indicated that: (a) the poured-plate method resulted in a higher yield of β haemolytic streptococci than any enrichment method or a surface-streaking method; (b) enrichment of swabs in Pike's broth increased the yield of streptococci as compared with simple streaking on a blood agar plate, especially with group B haemolytic streptococci; (c) a commercial enrichment broth was tested and found to be unsatisfactory as a culture medium. Colony counts indicated that larger numbers of streptococci were obtained from children with symptoms than from carriers. Antistreptolysin O antibody titres were found to rise significantly in many instances of the carrier state, thus indicating a state of sub-clinical infection, but the evolution of the antibody did not correlate well with the continuation or disappearance of the carrier state. An increase of the antibody was sometimes found in non-carriers, probably indicating a transient sub-clinical infection between the monthly swabbings. *H. Stanley Banks*

SCOTT, R. F., THOMAS, W. A. & KISSANE, J. M. **Rheumatic Pneumonitis: Pathologic Features.** *J. Pediatrics.* St. Louis. 1959, Jan., v. 54, No. 1, 60–67, 8 figs. [15 refs.]

Cancer

WYNDER, E. L. **Laboratory Contributions to the Tobacco-Cancer Problem.** *Brit. Med. J.* 1959, Feb. 7, 317–22, 7 figs. [55 refs.]

This report is a review of work being done in laboratories all over the world. Since the materials used in smoking are thought to include carcinogens which are active in man, laboratory experiments have been directed towards identifying the carcinogenic contents of tobacco and showing them to be active in animals. Exposure of mice to tobacco smoke has not resulted in the production of bronchogenic tumours by inhalation although damage to lung and bronchial tissue has been observed. The heavy mortality in mice living in high concentrations of tobacco smoke handicaps such experiments. One experiment on rats injected with tobacco smoke condensate and tubercle bacilli into the hilum has resulted in carcinomas in 2 out of 8 animals so treated. Carcinomas have been produced on the skin of rabbits and several strains of mice by application of tobacco smoke condensate. In mice such results have been achieved with condensates of cigarette, cigar and pipe smoke.

In a large biological study the author and his colleagues have shown that most of the carcinogenic activity of these condensates is in the fraction (1·7%) of the total tar which is eluted with carbon tetrachloride from the neutral tar. In 10% concentration this fraction produced cancers in all animals to whom it was applied. Chemical studies incriminate the higher polynuclear substances as the carcinogenic agents present in tobacco condensates. Although in unburned tobacco there are small amounts of some higher aromatic polycyclics, formed during curing, most of the

polynuclear substances form during burning. The production of the carcinogens appears to be related to the maximum temperature at which this occurs and the duration of temperatures at given levels.

Dose-response studies on mice have shown that not only is there an optimum exposure level to cigarette tar for the production of carcinomas but also a minimum level—probably about one-third of the optimum. This offers an explanation of the inability of some workers to produce skin cancers with tobacco tar. Comparison of types of tobacco and of filtered and unfiltered cigarettes shows that filters and some brands result in less total tar than no filters and other brands. However, no differences have been shown between filtered and unfiltered or different brands in the carcinogenic activity per unit of resultant tar.

The work described suggests 3 important possible ways of reducing the risk of lung cancer in smokers. First, the tar content could be reduced by use of filters, which must be mechanically efficient, and selected tobaccos. This can be achieved without delay and the author shows some progress made by manufacturers; between 1957 and 1958, 6 filters and 6 brands tested all showed a reduction of 4–40% in their tar content. Second, the temperature at which tobacco burns during smoking should be reduced to a level to minimize the formation of polynuclear substances. Third, the polynuclear content of the smoke condensate might be reduced by use of catalysts, if suitable catalysts can be found. The author and his colleagues are currently engaged on research relevant to the second and third measures. *E. A. Cheeseman*

DOLL, R., HILL, A. B., GRAY, P. G. & PARR, E. A. **Lung Cancer Mortality and the Length of Cigarette Ends. An International Comparison.** *Brit. Med. J.* 1959, Feb. 7, 322–5, 1 chart.

If the many hazards of making international comparisons of mortality rates and statistics about tobacco consumption are accepted, there is in these data evidence of an association between mortality attributed to cancer of the lung in men and cigarette consumption per head of the population. Using data from 16 countries the authors calculated a correlation coefficient of $r = 0{\cdot}76$ between the standardized death rate in 1952–4 and the number of cigarettes consumed per adult in 1930. They discuss the various limitations of this analysis, which need not be considered here, and point out that this relationship has 2 main exceptions. In both Japan and the U.S.A. the death rate was rather lower than would have been expected from the linear regression of mortality on cigarette consumption. It has been suggested that the practice of throwing away a large unsmoked cigarette butt by smokers in the U.S.A. may contribute to the relatively low mortality and a recent survey there has provided factual data about this habit. This paper provides similar information for England and Wales.

A systematic random sample of 200 members of the civilian population of England and Wales was obtained from the current Electoral Register. Letters were sent to the sample members asking for particulars about usual smoking habits, and, further, asking cigarette smokers to collect in a tin, forwarded with the letter, the butts of all cigarettes smoked on the day after the letter was received. Of the 200 sample members, 81 men and 99 women replied; of these 33 men and 70 women said that they were not then smoking, 38 men and 29 women smoked only cigarettes, 4 men smoked cigarettes and a pipe and 6 men smoked only a pipe. The butts returned by the cigarette smokers amounted to about 80% of the number said to be usually smoked in a day.

On receipt the 772 butts were measured and the average length was $18{\cdot}7 \pm 0{\cdot}4$ mm., that is a little over a quarter of an ordinary length cigarette (70 mm.). Comparisons of mean length of butt were made between those received from different sexes, age-groups of men, groups of people smoking different usual daily amounts, groups smoking filter- and non-filter tipped cigarettes. The only material difference found was between the sexes (19·3 mm. for men and 17·3 mm. for women).

Data in the U.S.A. survey were obtained by collecting 4,283 butts from ashtrays in homes, offices and restaurants and picked up in streets, stations and parks in towns scattered over the country. Here the mean length was 30·9 mm. and from the method of collection is likely to underestimate slightly the average length of butt at the time of rejection. Nevertheless the difference between the U.S.A. and the English estimates is striking, representing, as it does, about 15% of the length of an ordinary cigarette. Comparison of the 2 frequency distributions is naturally more informative. Out of every 3 butts in the British data 2 were less than 20 mm. in length compared with less than 1 in 10 in the American. Only 1 in 40 was as long as 30 mm. in the British data compared with about 1 in 2 in the American. *E. A. Cheeseman*

LYONS, M. J. **Presence of 1,2,3,4-Dibenzopyrene in Cigarette Smoke.** [Correspondence.] *Nature.* 1958, July 19, v. 182, 178.

1,2,3,4-dibenzopyrene has been described as a carcinogenic agent of considerable potency, and the author has now recognized its presence in cigarette smoke. 1·6 mgm. was recovered from 100 cigarettes smoked to a stub length of 1·5 cm., which is about the same concentration as for 3,4-benzopyrene. Small quantities have also been found in petrol and the exhaust products of Diesel engines, but not in general urban atmospheric soot, in which 3,4-benzopyrene occurs in relatively high concentration.

"Thus, it would appear that the urban-dwelling cigarette smoker has an exposure to 1,2,3,4-dibenzopyrene in a concentration not realized by his non-smoking neighbour." *Charles Wilcocks*

HAMMOND, E. C. **The Association between Smoking Habits and Death Rates.** *Amer. J. Pub. Health.* 1958, Nov., v. 48, No. 11, Pt. 1, 1460–68. [42 refs.]

In the prospective studies of smoking in relation to cancer of the lung carried out by HAMMOND and HORN [this *Bulletin*, 1954, v. 29, 1231] in the U.S.A. and DOLL and HILL [*ibid.*, 1954, v. 29, 1059; 1957, v. 32, 145] in the U.K. it was found that some other causes of

death as well as lung cancer were associated with cigarette smoking (though none to the same degree as lung cancer). This has led BERKSON (*J. Amer. Statistical Ass.*, 1958, v. 53, 28) to argue that the evidence is suspect for it is incredible that smoking should cause many diseases. It is not, however, necessary to believe that it does cause all such diseases. It is possible for an environmental factor which has nothing to do with the original causation of a disease to increase death-rates from that disease. For instance, the London fog of 1952 increased the death-rate not only from respiratory diseases but from heart diseases and many other causes [this *Bulletin*, 1955, v. 30, 615]. Influenza epidemics likewise affect mortality over a wide range of diseases.

There is certainly nothing unusual about one agent (including such a factor as a drug or antibiotic) having a multiplicity of effects (good or bad) on the human body. Considering the complex chemical composition of tobacco smoke it would not be surprising to find that chronic exposure to it had many harmful effects. Thus it has been shown experimentally to inhibit ciliary action and to produce histological changes in the bronchial epithelium [*ibid.*, 1957, v. 32, 448]. It contains at least one known carcinogen for laboratory animals and the presence of several others has been reported. It has a number of acute effects on the human circulatory system, including increase in heart rate and blood pressure and constriction of the peripheral blood vessels. Clinical studies have suggested that smoking decreases the effectiveness of treatment for peptic ulcers and may promote the breakdown of healed or quiescent pulmonary tuberculosis [*ibid.*, 1957, v. 32, 238]. It is not, therefore, inconsistent with biological and medical knowledge that cigarette smoking should increase mortality from several different diseases, whether directly or indirectly. The fact, then, that it appears to do so in these enquiries does not cast doubt on the belief that it is a factor of considerable importance in the causation of lung cancer.

A. Bradford Hill

See also p. 462, DEICHMANN, MACDONALD, COPLAN, WOODS & ANDERSON, **Para Nitrobiphenyl, a New Bladder Carcinogen in the Dog.**

Dental Hygiene

NEVITT, G. A., WITTER, D. H. & BOWMAN, W. D. **Topical Applications of Sodium Fluoride and Stannous Fluoride.** *Pub. Health Rep.* Wash. 1958, Sept., v. 73, No. 9, 847–50. [17 refs.]

There have been reports which suggest that stannous fluoride is more effective than sodium fluoride in reducing the solubility of powdered enamel, and some further reports suggest that stannous fluoride applied topically to teeth in the mouth is more effective in reducing dental caries than is sodium fluoride similarly applied.

In 1955–7 the authors carried out an investigation in 2 areas in Oregon, U.S.A.—children of 9–14 years of age having a 2% stannous fluoride solution applied to the teeth in 2 mouth quadrants, and a similar number of children (almost 300) having an application of 2% sodium fluoride. The untreated quadrants served as controls. The findings 16 months after the initial examination are described by the authors in these terms:—

"1. The incidence of dental caries in permanent non-carious teeth was significantly lower in mouth quadrants treated with either stannous fluoride or sodium fluoride than in untreated quadrants.

"2. The findings relative to the comparative effectiveness of stannous fluoride and sodium fluoride were inconclusive."

Robert Weaver

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order: General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology

PRACTITIONER. 1958, Aug., v. 181, No. 1082, 133–83, 7 figs. [Numerous refs.] **Industrial Medicine.**

In the editorial comment on the first page of this issue of *The Practitioner* the remark is made that "In these days of increasing complaints about the diminishing scope of general practice, it is particularly appropriate that attention should be drawn to the openings offered to the general practitioner in this field of medicine." The symposium which follows that introduction emphasizes the part that general practitioners can take in industry.

In the first paper (*The General Practitioner in Industrial Medicine,* pp. 133–142) Stephen TAYLOR remarks that in 1955 medical officers were employed whole-time at 421 factories, and part-time at 4,198 factories; the general practitioner, in fact, is already implicated in the industrial scene, but he has much to learn. Taylor describes the Harlow experiment in which, at one of the new towns, 35 firms are members of a joint organization to take care of the health of the workers; the conditions are special and the initial costs were considerable, but the venture is proving successful.

The second paper, by A. MEIKLEJOHN, is on *Pneumoconiosis in General Practice* (pp. 143–150). The main aspects which affect the family doctor are diagnosis and certification, advice on employment, rehabilitation and medical supervision. The author takes these points in succession, and discusses the difficulties which arise in law—for instance the fact that in middle-aged workmen after 30–40 years' work at the coal face or in foundries, seriously disabled by persistent breathlessness due to bronchitis and emphysema, it may be extremely difficult to prove that the condition comes within the present definition of a disease which entitles to compensation.

The third paper, by M. W. GOLDBLATT, relates to *Occupational Cancer* (pp. 151–163), and the author takes the reader briefly through the present ideas on the role of asbestos, haematite, nickel, "isopropyl oil", chromium and aromatic amines, ending with a note on carcinoma of the bladder.

F. F. HELLIER writes on *The Problem of Industrial Dermatitis* (pp. 164–169), emphasizing the special difficulties of diagnosis, and the importance of prevention.

R. C. BROWNE (pp. 170–175) briefly mentions some of the *Occupational Diseases due to Infections*—anthrax, leptospirosis, hookworm infection and others. J. M. BARNES (pp. 176–183) concludes the series with a paper on *Occupational Hazards arising from the use of Toxic Substances in Agriculture,* particularly the insecticides, of which the organic phosphorus compounds are perhaps the most important, though not the only dangerous substances.

[This collection of papers would serve as an introduction to a subject of growing importance, either to medical men who may meet cases in general practice, or to those who though not personally involved may need a brief conspectus of part of the subject.]

Charles Wilcocks

BRITISH J. INDUST. MED. 1959, Jan., v. 16, No. 1, 70–75, 1 fig. **Occupation and Mortality. [Miscellanea.] [i] Filial Mortality** [HEADY, J. A.], 70–73. **[ii] Mortality in Mining and Quarrying Occupations** [REID, D. D.], 73–4. **[iii] Mortality in Transport Occupations** [CORNWALL, C. J.], 74–5.

These 3 papers, based on the Occupational Supplement of the Registrar-General, discuss some aspects of the problem of occupational risk which might interest industrial Medical Officers.

Heady reviews the mortality among infants by occupation of the father. Neonatal, post-neonatal and the stillbirth rate all increase as the social class of father decreases from I to V. The same progression was found for 5 important causes of infant deaths. There was a considerable variation in the size of the infant mortality between occupational groups and of the 10 groups with the highest infant mortality 2 were from social class III and 2 from social class V and of the 10 groups with the lowest infant mortality one was from social class III. The infant mortality of these 20 groups is compared with the standardized mortality ratio for ages 20–64 for respiratory tuberculosis, chronic heart disease, pneumonia and bronchitis, which have a marked social class gradient. Generally the mortality for these causes was low where the infant mortality was low and high where the infant mortality was high but there were some interesting exceptions. Heady discusses the reliability of the occupational data and the difficulties arising from change of job and those arising from the fact that the data on deaths and population come from 2 different sources, the consequence being that the occupation on the death certificate may differ from that given in the census return.

The validity of the death rates in the mining population has been questioned, particularly comparisons between different occupations within the industry. Reid reviews the difficulties of obtaining a true death rate, the chief of which is the actual occupation of the dead man. A recent investigation [this *Bulletin,* 1958, v. 33, 1143] comparing occupations showed that there were serious discrepancies between that given on the death certificate and the actual occupation followed at the time of death. Many men were described as coal-face workers who were not employed in this capacity. It seems that coal-face workers have a lower mortality than that ascribed to them in the occupational supplement. Movements within the industry are factors which affect the death-rate and it is, generally, the younger and fitter men who leave the industry when work

becomes scarce. It is evident that caution is needed in interpreting the specific death-rates for occupational groups within the mining industry. Accidents and dust diseases are undoubtedly hazards of importance.

Transport workers form another large occupational group which gives rise to difficulties in interpretation of death-rates. Cornwall outlines these difficulties. Among railway workers the ticket collectors have a high mortality mainly because this occupation is one to which men rejected from other grades of work are posted. Misstatements of occupation affect comparisons between groups of transport workers. Medical selection in the case of holders of a public services vehicle licence influences the mortality rate of this group, which is low. Rates for water transport workers are affected by omissions in the census returns for the merchant navy.

W. J. Martin

American Indust. Hyg. Ass. J. 1958, Apr., v. 19, No. 2, 154–63. [Numerous refs.] **Hygienic Guide Series.**

This is an addition to the existing series of short dogmatic statements on various noxious substances and relates to:—lead and its inorganic compounds, ethylene dibromide, methyl bromide, natural uranium, amorphous silica, and asbestos. In each section information is given on maximum allowable atmospheric concentrations, severity of the hazards, tolerance to short exposures; on the significant properties of the substance; on industrial hygiene practice in relation to it; and on specific procedures to be adopted in relation to exposed persons. For each substance a short list of references is given. Further lists are given in subsequent issues of the same journal.

These Hygienic Guides may be obtained from the American Industrial Hygiene Association, 14125 Prevost, Detroit 27, Michigan, U.S.A., at 25 cents a copy. They now cover 56 substances, and later additions will be published.

Charles Wilcocks

Associated Industries of New York State, Inc. **Fourth Noise Conference.** *Amer. Indust. Hyg. Ass. J.* 1958, Oct., v. 19, No. 5, 386–437, numerous figs. [14 refs.]

The first of the 16 papers published on the Conference reviews progress in the United States since 1950 in the identification of intensity, frequency and duration of noise which "at certain high levels of intensity presently existing in industry" can cause loss of hearing. The need for better methods of evaluating disability from hearing loss is stressed in the light of medico-legal responsibilities of employers under various State laws. Other papers deal with this legislation in the States of New York and Wisconsin and consequent hearing conservation measures adopted by large industries in those States. Several companies have instituted pre-employment and "in service" hearing tests, partly to protect the worker and partly to protect their own interests under the Workmen's Compensation Law. Employers are realizing that loss of hearing is as important a problem as that of accidents to their workers. In the paper on hearing conservation in Wisconsin, reference is made to a school survey which indicated that from 5% to 10% of the children had hearing losses and 3% were in need of medical care for their hearing. Over 100,000 children in 47 States attend day schools for the deaf. In Wisconsin, it is estimated that 27 in 100 newly engaged workers have hearing losses on initial employment. 300 centres have been established in the State for hearing examinations; large industrial plants retain the services of consultant otologists. The importance of protective equipment, such as muffs and earplugs, is stressed, but there is reluctance on the part of the worker to use it (as is found, of course, with other items of protective clothing).

5 papers deal with various aspects of industrial noise sources, instruments and methods of measurement of noise, and the medical and technical personnel required to carry out a measurement programme; control of noise, by quietening the source, substituting less noisy operations or machines, isolating the source or the worker and reducing exposure time; and the advantages and limitations of acoustic treatment by sound absorption, isolation and insulation. Noise specifications are suggested to assist manufacturers and users in defining maximum acceptable noise levels for equipment to be used in specific installations.

Finally, there is a group of papers concerned with specific industrial processes, in which the operations causing excessive noise and the measures taken to suppress it are described. Details are given, for example, of enclosures for machines used to crush stone, ore, slag, etc., and mufflers for exhausters and boosters in chemical works and for jet engines in aircraft undergoing ground tests.

Although the medical implications of noise in industry are touched upon, the technical application of control measures is the predominant feature of these papers.

A. H. Phipps

Keatinge, G. F. & Laner, S. **Some Notes on the Effects of Excessive Noise on the Hearing of a Group of Workers.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 273–5, 1 fig.

Noise measurements in a group of riveting and metal fabricating shops showed that the workers were exposed to sound pressure levels ranging from 115 to 128 decibels (db) with peak intensities occurring in the frequency range 1,000 to 2,000 cycles per second.

Pure tone audiometry was carried out on 2 groups of workers aged 40 or less, the age selection being made to minimize the complicating factor of presbycusis. One group, comprising 20 subjects, had not been exposed to intense noise for any appreciable length of time, and the other group, totalling 63 subjects, had been exposed to the noise in the workshops for periods up to 7 years. The findings for both groups are expressed in terms of a percentage rating for speech hearing loss.

On this basis, the results are interpreted as indicating that the greatest speech hearing loss occurs during the first 3 years of exposure and that after this period the rate of deterioration of hearing is reduced. In fact, workers with 6 and 7 years' exposure are shown to have a speech hearing loss less than those with 3 to 5 years' exposure. It is suggested that the adoption of ear

protective devices is of little value if the worker has already been exposed to intense noise for a period of 3 years.

[As it was apparently not possible for the audiometry to be carried out before noise exposure began each day, it is probable that temporary deafness effects have influenced the results.

The audiometry is interpreted in terms of a speech hearing loss, derived from the measured air conduction losses at 512, 1,024, 2,048 and 4,096 cycles per second, the middle 2 frequencies being given a weighting more than double that given to 4,096 cycles per second. The latter frequency is, of course, that at which the greatest occupational hearing damage normally takes place. The interpretation of the audiometry might have been somewhat different if hearing damage, rather than capacity to hear speech, had been used as the criterion.

The implications of the hypothesis put forward are so important that, as the authors admit, further evidence should be obtained before it is accepted.]

D. E. Hickish

WÜNSCHE, O. Zur Pathogenese und Prophylaxe der Druckfallkrankheit des Höhenfliegers. II. Mitteilung. Der Einfluss narkotischer und sedativer Mittel auf die intravasale Gasblasenbildung im Drucksturzversuch. [**Pathogenesis and Prevention of Decompression Sickness in Airmen. II. Influence of Narcotic and Sedative Agents on the Formation of Intravascular Gas Bubbles in Experimental Studies**] *Internat. Ztschr. f. Angewandte Physiol.* 1958, v. 17, No. 4, 303–15, 8 figs. [27 refs.]

In the study of the pathogenesis of decompression sickness the variability in the localization, intensity and latent period before onset of the symptoms present a problem which cannot be solved satisfactorily from a knowledge of the aetiology of the condition. For this reason it is suggested that investigation of the part played by exogenous factors such as muscular activity or trauma and the endogenous factors such as individual constitution or disposition may throw light on the problem. The author of this paper describes and discusses some of the relevant literature on the importance of these factors in decompression sickness and presents the results of his own experiments on rats. In these investigations the animals were submitted to rapid decompression after having been given a narcotic or sedative and the formation of intravascular gas bubbles was then compared with that of control untreated rats. The results are set out in figures and a table gives a list of the different drugs which were administered. It was found that with certain exceptions the narcotic or sedative treatment brought about a lessening of gas bubble formation as a result, it is stated, of the altered metabolism produced by the medication.

M. E. Delafield

THOMSON, J. D. & YOUNG, A. B. **Aseptic Necrosis of Bone in Caisson Disease.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 270–72, 2 figs. [11 refs.]

An account of a case.

LANE, R. E. **Chronic Bronchitis and Occupation.** *Brit. J. Tuberculosis.* 1958, Jan., v. 52, No. 1, 11–18. [20 refs.]

Chronic bronchitis may be a disease with many causes, among which occupational factors such as dust, fume, change of temperature and exposure to weather are mentioned.

Epidemiological studies reveal that coal-miners, gas workers, furnace dismantlers and steel workers—all of whom may be exposed to dust and fume—suffer unduly from chronic bronchitis. A few dusts such as vegetable and siliceous dusts may produce chronic bronchitis and most dusts probably aggravate an existing bronchitis. Some, such as pure limestone, do not appear to produce any damage to the lung. Exposure to high temperatures, changes of temperature and bad weather have all been suggested as possible causes or aggravants. As non-occupational factors also cause or aggravate chronic bronchitis, it is difficult to ascertain the importance of occupational factors in the aetiology of this disease.

R. S. F. Schilling

FLETCHER, C. M. **Disability and Mortality from Chronic Bronchitis in relation to Dust Exposure.** *Arch. Indust. Health.* Chicago. 1958, Nov., v. 18, No. 5, 368–73. [13 refs.]

The author summarizes the main facts about chronic bronchitis in Great Britain that emerge from the mortality and morbidity statistics. He comments on the sex incidence, urban/rural and social class differences and occupational factors and indicates their possible interpretation in the light of tobacco smoking and atmospheric pollution. He then considers a number of investigations carried out in different centres to assess the aetiological importance of atmospheric pollution and dust exposure and points out certain discrepancies in the findings in different surveys. He advocates more prevalence and long term follow-up studies of appropriate populations in order to elucidate these factors and urges that studies similar to those now being pursued in Great Britain should also be conducted in the United States in order to show whether the apparent difference in prevalence between the 2 countries is real or due to different fashions in diagnosis and death certification.

I. T. T. Higgins

HIGGINS, I. T. T. **Tobacco Smoking, Respiratory Symptoms, and Ventilatory Capacity. Studies in Random Samples of the Population.** *Brit. Med. J.* 1959, Feb. 7, 325–9. [28 refs.]

This study on a random sample of 734 men aged 25–64 drawn from the population of the Rhondda Fach, Vale of Glamorgan (South Wales), Leigh (Lancashire) and Annandale (South-west Scotland), is concerned with the relationship between tobacco smoking to respiratory symptoms and to ventilatory capacity. The total sample was made up of 16 sub-groups defined by place, age, occupation (miners, including ex-miners and non-miners), X-ray category of simple pneumoconiosis. Not all possible sub-groups were necessarily represented in all places and of the sample drawn 90% were seen. Ventilatory capacity was measured by the indirect maximum

breathing capacity test (MBC). Smoking habits were classified in the way suggested by DOLL and HILL [this *Bulletin*, 1951, v. 26, 49].

In 2 of the 16 sub-groups there were no non-smokers; in 13 of the other 14 the mean MBC was higher for non-smokers than for smokers. The weighted average difference was 9 litres per minute and the observed mean differences ranged from −11 to +27 litres per minute. There was no apparently consistent trend in MBC with increasing tobacco consumption. Only in 2 groups, the elderly miners of Rhondda with and without simple pneumoconiosis, did the heavy smokers have a worse MBC result than the light smokers. When the data relating to men aged 55–64 from different areas were pooled, there was evidence of a decreasing mean MBC with amount smoked in each of the resulting 4 occupational X-ray groups. Thus for non-miners who were non-smokers the mean in litres per minute was 100·3, for those who smoked 1–14 gm. per day it was 90·6 and for 15 gm. and over per day it was 89·1. Corresponding means for miners and ex-miners were 81·1, 74·5 and 69·6 litres per minute respectively for those of pneumoconiosis category 0; 93·1, 76·7 and 75·8 litres per minute respectively for those with simple pneumoconiosis and 84·0, 70·7 and 63·8 litres per minute respectively for those with progressive massive fibrosis (PMF). Although these means suggest a downward trend with amount smoked, only the differences between smokers as a whole and non-smokers are apparently significant at conventional levels.

The comparison between non-smokers, light smokers and heavy smokers in terms of respiratory symptoms is limited to 393 men who formed the sub-samples of men aged 55–64 in Leigh, Vale of Glamorgan and Annandale. There was a clear relationship between smoking and persistent cough and sputum; this symptom for part of the day most days for at least 3 months in the year was recorded for 6·1% of non-smokers, 19·7% of light smokers and 42·3% of heavy smokers. Between non-smokers and smokers there was also a difference for chest illness, wheezing, breathlessness and "chronic bronchitis" defined as persistent sputum and at least one chest illness in the last 3 years; in non-smokers the percentages recording these were respectively 3·0, 15·2, 18·2 and 0; in smokers they were about 24, 52, 32 and 16. If the pipe smokers in this group are considered separately their percentages with the 4 "symptoms" above are respectively 18·2, 41·6, 24·7 and 10·4, that is, intermediate between smokers and non-smokers.

E. A. Cheeseman

MINETTE, A. & VAN WIJMEERSCH, L. Standardisation d'une technique d'aérosolisation de l'acétylcholine. [**Standardization of Technique for Nebulizing Acetyl Choline**] Reprinted from *Acta Allergologica*. 1958, Suppl. 5, 222–33, 4 figs.

The authors describe a technique for measuring accurately the amount of an aerosol effectively inhaled. They indicate that there is considerable variation from person to person in the minute ventilation during inhalation of an aerosol and that this cannot be predicted from the resting ventilation. *I. T. T. Higgins*

MINETTE, A. & VAN WIJMEERSCH, L. Effets des aérosols d'acétylcholine chez les houilleurs. [**The Effects of Acetyl Choline Aerosols in Coal-miners**] Reprinted from *Acta Allergologica*. 1958, Suppl. 5, 234–51, 2 figs. [10 refs.]

The authors have investigated the effects of aerosols of acetyl choline in 104 coal-miners, 35 healthy non-mining controls and 36 patients with asthma or chronic bronchitis of non-industrial origin. A reduction of 10% or more in the forced expiratory volume or a cough reaction were the criteria of a positive reaction. There appeared to be no significant correlation between a positive response to acetyl choline and

(1) complaints of cough or breathlessness when working in dusty atmospheres,
(2) physical signs in the chest or
(3) X-ray category of pneumoconiosis.

A positive test was, however, correlated with lung function, the frequency of reactions being significantly greater in those with a timed vital capacity of less than 50% or a residual volume/total lung volume of over 45%. *I. T. T. Higgins*

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Communication No. 152. Les lésions élémentaires de la pneumoconiose des houilleurs belges. Confrontation entre les documents anatomo-pathologiques et l'anamnèse professionnelle. [**Pneumoconiotic Lesions in Belgian Coal-Miners; Correlation between Pathological Findings and Working History**] [MEERSSEMAN, F.]. 1958, Apr. 15, v. 13, No. 3, 35 mimeographed pp., 16 figs. (14 on 8 pls.). [32 refs.]

The author examined the lungs of 40 Belgian coal-miners; in 36 pseudotumoral masses were found in addition to other changes, but the pseudotumoral masses are not discussed in this paper. Detailed enquiry into the working history of 27 of the men allows correlation of the lesions with the type of dust encountered.

"Simple collections of dust particles, with and without fibrosis, are as common in coal-miners as in men working in rock. Dust aggregations with marked focal emphysema are found almost exclusively in coal workers and are almost uniformly distributed throughout the lung.

"Fibrohyaline lesions, on the other hand, are localized near the pseudotumoral masses; they are common in rock workers but more rare in coal workers, and are seen only as fibrohyaline masses in the latter. Fibrohyaline nodules, whether circumscribed or not, have been found only in men exposed to rock dust. Classical silicotic nodules (circumscribed fibrohyaline nodules) were observed in only 5 cases, of which 2 also showed tuberculous lesions.

"The pneumoconiosis of coal workers in Belgium therefore resembles that of Wales, and differs in the rarity of the classical silicotic lesions from the conditions described in Germany, and by FRÜHLING and CHAUMONT in the miners of Lorraine. These differences are more explicable if the occupational history of the men is investigated.

"The pathogenesis of the fibrohyaline lesions is obscure, and further research is needed to define the role of superinfection with tuberculosis. In view of the rarity of fibrohyaline nodules in coal workers the theories advanced to explain the formation of silicotic nodules do not apply satisfactorily to the development of coal-workers' pneumoconiosis."

[The translation is from the author's summary in French.] *Charles Wilcocks*

SOMA, K. **[Study of Erythrocyte Sedimentation Rate of Colliers]** *Igaku Kenkyu.* Fukuoka. 1958, Oct., v. 28, No. 10, 3933–54, 11 charts. [128 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"Erythrocyte sedimentation rate (ESR) of colliers, 5610 males, 195 females and 332 applicants, was studied from various angles.

"1. ESR of the colliers, compared with that of other general populace, is in every age group significantly accelerated, in males as well as in females.

"2. ESR of pit-workers is more accelerated than that of surface-workers. Of the pit-workers it is most accelerated in coal-getters, the next being that of drillers.

"3. ESR of the colliers increases with advance in age, but no difference with respect to duration of employment in the same age groups.

"4. ESR of new applicants is not different from that of general populace. But one month after employment ESR shows significant acceleration which is more conspicuous in the pit-workers than in the surface-workers and in the coal-getters than in the drillers. This fact indicates that the change of blood quality occurs in rather early stage of employment and the acclimatization to the new environment takes place pretty soon.

"5. The fact that ESR of colliers is accelerated seems probably due to physiological changes caused by hard muscular labor in the pit of high temperature, humidity and air pressure."

CARLÍN, C. E. Caracteristicas de la silicosis en las minas del Perú. Estudio epidemiológico preliminar. **[Characteristics of Silicosis in Peruvian Mines. Preliminary Epidemiological Study]** *Rev. Med. Exper.* Lima. 1957, Dec., v. 11, Nos. 1/2, 1–27, 3 figs. on 2 pls. English summary.

This paper is a study of 22 Peruvian mines. The products were coal, copper, lead, silver, zinc, gold, tungsten, iron and vanadium.

Investigations were made of the silica content of the atmospheric dust and the size of the silica particles in various locations. 11,684 underground and surface miners were examined medically.

There is a close association between the incidence of silicosis and the concentration of free silica in the atmosphere and between the incidence and the period of exposure.

In mines with a median figure of less than 5% of silica in the atmospheric dust and 6·9 million particles per cubic foot of air the incidence of silicosis was 2·4 per 1,000 miners with less than 5 years' employment in the mine but it was 30·9 per 1,000 among those who had worked between 5 and 14 years. In mines with more than 50% of free silica in the dust and 4·8 million particles per cubic foot of air the figures were 30·7, 48·3 and 76·9 per 1,000 among those who had worked fewer than 5, 5–14·9 and over 15 years respectively.

A series of tables give details and another classifies the mines according to the number of particles of silica per cubic foot of air. The results are similar in demonstrating the close relationship between the occurrence of silicosis, the dust concentration and the period of exposure.

Of the 7,306 miners examined with less than 4 years' service, 94 (1·3%) had silicosis. In 3 patients the length of exposure had been short, namely 7, 13 and 16 months. In all 3 the concentration of silica in the mines where they worked had been high. *Allen Daley*

HAFERLAND, W. Graphitstaublunge und Silikose. **[Graphite Pneumoconiosis and Silicosis]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1957, v. 16, No. 1, 53–62, 6 figs. [10 refs.]

The paper gives in great detail a pathological description of the lungs of a man who had worked for several decades first as a potter and then as a graphite grinder, and finally for 11 years in the manufacture of hydrofluoric acid from cryolite. At the age of 78 he died of a thrombosis of a leg vein and at autopsy he was found to have suffered from advanced pyelonephritis due to hypertrophy of the prostate.

The lungs were found to be black, with large and small fibrotic masses and cavities, but no signs of tuberculosis were found. A number of illustrations show hyaline dust nodules and other fibrotic changes. Chemical analysis of the dust showed much graphite, quartz and oxides of iron and aluminium.

There is a long discussion on the relative importance of graphite and quartz as causes of the fibrosis and the author concludes that graphite is harmless and that all graphite pneumoconioses known until now are in fact graphite silicoses caused by quartz which occurs in all graphite dusts. *G. Nagelschmidt*

GRAVENKAMP, H. Über den histologischen Nachweis silikotischen Gewebes im Sputum bei kavernösen Silikotuberkulosen. **[The Histological Demonstration of Silicotic Tissue in the Sputum in Cavitating Silicotuberculosis]** *Beiträge z. Silikose-Forschung.* 1958, No. 52, 1–16, 7 figs.

The paper describes the first results of an attempt to confirm the presence of silicosis together with actively progressing tuberculosis by sputum investigations. The method used was to centrifuge the sputum after adding formalin and sublimate, to dehydrate the sediment, embed it in paraffin and to stain it by the van Gieson method. A number of illustrations are given which show pieces of silicotic hyaline tissue with areas of necrosis, pigmentation by carbon and leucocytes. Repeated investigations of material from the same patient may be

required, as sometimes a positive result was preceded by up to 3 negative tests.

A comparison of histological sputum analyses with clinical observations and working histories showed reasonable agreement although there were sputum-negative cases of what was later confirmed by autopsy to be silicosis.

The case of a woman is described in detail who had worked in the ceramic industry and was treated for tuberculosis. The X-ray had shown cavitation but no obvious silicosis. While in hospital, this patient produced a piece of tissue in the sputum which was identified by the author as a silicotic lesion and as a consequence the patient obtained compensation for silicosis.

It is concluded that while negative results do not prove the absence of silicosis, positive results can be of diagnostic value in the hands of experienced pathologists, and a more general use of the technique is recommended. *G. Nagelschmidt*

EINBRODT, H. J. Der Aufschluss des Gewebes mit Formamid als neue Methode zur histochemischen Darstellung anorganischer Substanzen mit Beispielen an Schnitten aus silikotischen Lungen. **[Treatment of Tissues with Formamide as a New Method for Histochemical Preparation of Inorganic Substances, for example in Sections of Silicotic Lungs]** *Beiträge z. Silikose-Forschung.* 1958, No. 52, 17–54, 28 figs. [38 refs.]

The paper describes an adaptation for use on tissue sections of the technique of THOMAS and STEGEMANN [this *Bulletin*, 1955, v. 30, 237] of destroying lung tissue with anhydrous formamide at 135°C. in order to isolate the lung dust. The sections are kept in place by silicone-coated platinum mesh and are treated with formamide in a specially designed glass apparatus for about 8 hours. The whole technique is described in great detail with illustrations of the equipment used and of the results obtained.

Data are presented for 7 silicotic lungs where size distribution and quartz content of the dust in silicotic nodules, assessed from sections, are compared with similar data for dust isolated from the whole lung. In the sections the quartz was estimated by phase contrast dispersion staining and in the whole dust isolated from the lungs it was determined in the same way as well as by calculation from a chemical analysis of the dust. The size distributions of total dust and quartz are given in tables and graphs.

Neither the size distribution nor the quartz content of the dust in the silicotic nodules were markedly different from the dust in the whole lungs. Quartz was found in every case, and 80 to 90% by number of all dust particles were below 4 microns in size.

G. Nagelschmidt

VYSKOCIL, J. & KADLEC, K. **The Influence of Androgens on the Development of Silicotic Granuloma.** *Rev. Czechoslovak Med.* Prague. 1958, v. 4, No. 1, 20–28, 2 figs. [24 refs.]

To study the action of androgenic substances on the development of silicosis nodules, the authors, working in the Clinic for Occupational Diseases, Brno, Czechoslovakia, studied their effect on the growth of lesions produced by injecting a suspension of SiO_2 into the combs of cockerels and capons.

66 3-month-old cockerels were divided into 2 equal groups; 33 were castrated and the others were left in their natural state. 14 days after castration, from which there were no side effects, all the birds were injected at the base of the comb with 0·4 ml. of a 5% suspension of SiO_2 in which the majority of particles were from 1–3μ in diameter. A chronological study of the histological development of silicosis nodules was made by killing 2 birds from each group, first after 14 days, then after 2 months and thereafter at intervals of 14 days up to 6 months, when all surviving birds (13 cockerels and 12 capons) were killed. The comb, because of its rich blood supply, proved a highly satisfactory tissue for the production of silicosis nodules. The silicotic lesions developed more fully in the cockerels than in the capons. Thus they were encapsulated by thicker layers of connective tissue, which penetrated to the centre of the nodule, contained more fibrocytes and showed greater connective tissue changes in the walls of the blood vessels. *A. Meiklejohn*

MAKIYAMA, K. **[An Experimental Study on the Action of the Silicic-Acid-Containing Rock Powder inhaled in Animals, with special reference to the Effect of the Powder on the Reproductive Gland and the Suprarenal]** *Igaku Kenkyu.* Fukuoka. 1958, Oct., v. 28, No. 10 3955–72, 12 figs. (8 on 2 pls.) [35 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"It has become a matter for concern among an increasing number of medical workers that silicosis, producing pathologic changes not only in the lungs, but also in the endocrine system and the central nervous system, may cause a general dysfunction and accelerate aging.

"Recent advances in the study of this condition have made it possible to treat the collagen fibrils formed in the condition with the suprarenal hormone, the hypophysical hormone, ACTH and Cortisone.

"The author has studied the disease and related problems by giving for inhalation in rabbits some rock particles collected from a pit in a certain coal mine, and by examining afterwards the reproductive gland, the suprarenal and the lung in these animals.

"The rock particles used contained 76.04% of its weight of SiO_2 the particles were 50 to 60% of them no more than 2 μ in diameter and were contained in a concentration of 1850 to 2500 per cc of air in the dust chamber. The animals were kept inhaling the particles for 3 hours at a time on the average and examined in two groups:—(I) those so treated for 534 to 1284 hours and (II) those so treated for 477 to 566 hours and left alone for the subsequent 300 to 359 days.

RESULT

"The changes produced in the animals were as follows:

"1) Deterioration of the general condition and appetite; mild irritation of the air passage; weight loss in many cases; deterioration of estrus in the male animals and a reduced frequency of pregnancy and reduced number of newborn young in the female.

"2) A reduction in the number of interstitial cells and sperm cells in the testicles; a decline of spermatogenic function.

"3) Deterioration of the oogenic function of the ovaries and a reduction in the number of primitive and mature ova.

"The above-enumerated sexual disturbances and the resultant abnormal secretion of sex hormone are likely to result in premature old age.

"4) Histological changes in the adrenal cortex: a reduction in the thickness of the cortex and in the number of the cells of Zona glomerulosa; and vacuolation and thinning of those cells: a change in the distribution of cells in Zona fasciculata and their clarification; reduced and nonuniform stainability of the fat granules; a reduction in the amount of 17-Ketosteroid; and a functional decline of the cortex.

"The suprarenal cortex is closely related to the formation of collagen fibrils, so that its functional decline may promote the development of silicosis.

"5) Histologic changes in the lung: the appearance of granulomatous tubercles—most of these irregular- or oval-shaped and each with the rock particles deposited in a varying number in it mainly in the bronchi, in the perivascular lymph follicles, in the connective tissue, in the pleura, and in the septum of each alveolus.

"6) It appeared probable that the dust inhaled impaired the endocrine organs and upset the normal secretion of hormone and that these functional disorders promoted the development of silicosis and brought about a state of premature old age."

CLAEYS, C. & QUINOT, E. Considérations sur la biologie de la silicose. [**Observations on the Biology of Silicosis**] *Rev. Méd. Minière.* Sin-le-Noble. 1958, v. 11, Nos. 38/39, 15–23. [137 refs.]

Reported studies on the biological aspects of silicosis are numerous but they are not easily accessible as they are scattered throughout the world literature on the pneumoconioses. The purpose of this contribution is to review this body of knowledge and to present it in language suitable for non-specialist medical readers and scientists. The various hypotheses, chemical, physical and physico-chemical, are succinctly presented. Finally the authors give an account of recent work on serum protein absorption on the surface of silica crystals and of the related antigen-antibody, immunological hypothesis of the pathogenesis of silicosis.

A valuable up-to-the-minute bibliography of 137 references is appended. *A. Meiklejohn*

CURRAN, R. C. & ROWSELL, E. V. **The Application of the Diffusion-Chamber Technique to the Study of Silicosis.** *J. Path. & Bact.* 1958, Oct., v. 76, No. 2, 561–8, 5 figs. (4 on pl.) [14 refs.]

The paper describes experiments made to test the solubility theory of silicosis.

Fibrogenic and inert dusts were enclosed in capsules with porous membranes of pore size below 0·45 or below 0·1 micron and implanted subcutaneously into mice and guineapigs and intraperitoneally into mice. At monthly intervals up to 7 months after insertion the capsules were removed, sectioned and examined for tissue reaction, especially for production of collagen at the outside of the membrane.

Usually each animal received 2 capsules, one with 5 or 10 mgm. of a fibrogenic dust (tridymite or quartz), one with a similar dose of an inert dust (felspar or carbon black).

A few capsules showed a very strong reaction which could be seen to be due to coccal infection. Sterile capsules showed uniformly a minimum reaction irrespective of the nature of the dust or the length of time in the tissues. These observations are shown in illustrations. More than 50 negative results were obtained. In ancillary tests it could be proved that the membranes were freely permeated by silica and protein solutions and that in fact silica was lost from the capsules after 2 and 3 months. The membranes acted only as a barrier between cells and dust particles, and as no reaction was observed the authors draw the conclusion that contact of fibrogenic dust particles with cells is necessary to bring about the tissue reaction characteristic of silicosis. This is opposed to the silica solubility theory, according to which dissolving silicic acid causes the fibrosis; it is also opposed to the view that proteins of the extracellular fluids, denatured by contact with quartz, cause fibrosis [this *Bulletin*, 1954, v. 29, 634].

G. Nagelschmidt

CEPPELLINI, R. & PERNIS, B. **Presence of Plasma Globulins in the Hyaline Tissue in Cases of Silicosis.** *Nature.* [Correspondence.] 1958, Jan. 4, v. 181, 55–6, 1 fig.

Hyaline tissue in cases of silicosis contains appreciable amounts of non-collagenous proteins [this *Bulletin*, 1957, v. 32, 49]. These proteins constitute up to one-half of the total protein content of the original tissue. Various tests suggested the presence of proteins chemically related to beta or gamma plasma globulins. To learn whether plasma globulins existed in silicosis hyaline tissue, the authors investigated this material to discover if it contained proteins having the immunological properties of plasma globulins. Hyaline tissue was obtained from 3 cases of typical silicosis immediately after autopsy. The test material was carefully homogenized in saline. The serum of a rabbit previously immunized with normal human serum was absorbed twice with one-third of its volume of the homogenized and washed silicosis hyaline tissue. This preparation was then used as an antiserum for immuno-electrophoresis according to the technique of GRABAR and WILLIAMS (*Biochim. Biophys. Acta.*, 1955, v. 17, 67). The authors conclude that acellular silicosis hyaline tissue contains a globulin fraction which may be identified with a plasma globulin having antigenic properties and an electrophoretic mobility corresponding to that of beta or gamma globulin. They further submit that these results are consistent with the hypothesis [this *Bulletin*, 1959, v.

34, 347] that an antigen-antibody of properdin substrate precipitation plays a part in the genesis of silicosis hyaline tissue. *A. Meiklejohn*

SEIFERT, H. Über experimentelle Untersuchungen zur Matrizentheorie der Silikose. [**Experimental Investigations on the Matrix Theory of Silicosis**] *Staub*. Düsseldorf. 1958, July 1, v. 18, No. 7, 201–6, 7 figs.

The matrix theory of silicosis assumes that the crystal lattice of quartz acts as a matrix on which proteins are adsorbed. Experiments claimed to support this theory consist in observing ordered crystal growth (epitaxy) of certain amino acids evaporated *in vacuo* on freshly broken or etched quartz surfaces. Several illustrations, mainly of glycine and hydroxyproline on quartz. are given and in a lengthy discussion it is concluded that the development of silicosis is analogous to virus infection and is an example of applied biocrystallography. *G. Nagelschmidt*

NACHTSHEIM, D. Über die Einwirkung von Quarzstaub auf Esterase. Ein Beitrag zum Problem der katalytischen Beeinflussung des Stoffwechsels durch Quarzstaub. [**On the Effect of Quartz Dust on Esterase. A Contribution to the Problem of the Catalytic Effects of Quartz Dust on Metabolism**] *Beiträge z. Silikose-Forschung*. 1957, No. 50, 53–70, 6 figs. & 1 diagram.

Quartz had been found previously to increase the activity of pancreas esterase, and this effect had been tentatively explained as being due to adsorption and inactivation of an unidentified esterase inhibitor [BAUMANN, H., this *Bulletin*, 1956, v. 31, 43].

The present paper describes experiments which were designed to test this hypothesis and to assess its magnitude by measuring the dissociation of methyl butyrate. Quartz was allowed to come to equilibrium with esterase solution during 7 days; it was then centrifuged off and suspended in part of a new esterase solution. The activity of this quartz suspension in esterase was compared with that of esterase solution alone and with that of the suspension when quartz was removed after various periods of time.

Results are given in figures and graphs. They show the suspension to be the most active system and it is concluded that probably:

(1) esterase adsorbed on quartz remains fully active;
(2) the as yet unknown inhibitor is destroyed by adsorption on quartz;
(3) the effect is considerable; at a ratio of 2·7 parts of quartz to 1 of esterase an increase of 45% of the initial activity was observed after 75 hours of contact with quartz.

It is concluded that this is the first example of a catalytic reaction on metabolism which is shown by quartz but not, for instance, by $AlPO_4$ with quartz structure. It could be relevant for explaining the mechanism of silicosis. *G. Nagelschmidt*

PUCCINI, C. Silicosi "anodulari" ad evoluzione fibrosa interstiziale diffusa. [**"Anodular" Silicosis with Interstitial Fibrotic Evolution**] *Med. d. Lavoro*. 1958, Nov., v. 49, No. 11, 655–64, 6 figs.

The English summary appended to the paper is as follows:—

"The pneumoconioses here called 'interstitial anodular silicosis' are those histologically characterized by: *a*) a *focal interstitial coniosis* formed by small clusters of coniophages and silica, particularly around the bronchi and the arterioles and formation of reticular fibres; *b*) a *systemic interstitial fibrosis*, with bundles of various thickness with neither formation of sclero-hyaline nodules nor massive fibro-hyalinosis, with relatively moderate reduction of the respiratory surface (slight interstitial fibrosis), alveolar emphysema, diffuse bronchiolar lesions (hypertrophic metaplastic bronchitis) and arteriolar changes (obliterating productive arteritis). These silicotic fibroses show a relative autonomy in their histological expressions, as compared with pulmonary interstitial fibroses of different or unknown etiology and with chronic productive interstitial pneumonias. The clinical picture shows crisis of cyanosis and dyspnea, pulmonary hypertension and progressive respiratory insufficiency."

GHIRINGHELLI, L. & PERNIS, B. Aumento della produzione di anticorpi nei conigli trattati con tridimite per via endovenosa. [**Increase of Antibody Production in Rabbits after Intravenous Injection of Tridymite**] *Med. d. Lavoro*. 1958, Nov., v. 49, No. 11, 665–71, 2 figs. [21 refs.]

The English summary appended to the paper is as follows:—

"A mean 5-fold increase in antibody production was observed in rabbits intravenously treated with Tridymite dust (100 mg) and subsequently (15 or 30 days afterwards) immunized with crystalline ovalbumin. This was not observed in Rabbits intravenously treated with 100 mg of caolin or coal dust 30 days before the ovalbumin injections; in these animals the antibody production was only slightly higher than that of untreated controls.

"Obviously the treatment with crystalline silica determines a comparatively lasting stimulation of the antibody producing system so that the antibody production against antigens injected during the development of generalized experimental silicosis is increased.

"These results, together with those of other research work performed in our laboratory, may perhaps be explained with the assumption that lipopolysaccharides are being slowly but continuously liberated by the macrophages which have phagocytized the silica particles; these lipopolysaccharides might then exert an adjuvant action on antibody production acting more or less as the endotoxinlike lipopolysaccharides extracted by Landy (1957) from different mammalian tissues.

"Our observations are a further support of the assumption that immunological reactions play a role in the pathogenesis of silicosis, and may perhaps help to explain the increase of gamma-globulins usually observed in the sera of silicotic patients."

PERNIS, B., CLERICI, E. & BHEZZI, I. L'azione sui tessuti del quarzo racchiuso in cellette con membrane a micropori. [**Studies on the Action of Quartz-Containing Millipore Membrane Chambers introduced subcutaneously in Rats**] *Med. d. Lavoro.* 1958, Nov., v. 49, No. 11, 672–82, 5 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"In order to collect further information on the 'solubility theory' of silicosis, perspex chambers with millipore (0.3 μ) membranes were introduced in the subcutaneous space of rats, some of these chambers containing 50 mgr. of fine quartz dust. After 7 months the tissues around the chambers were examined: no differences were noted between the reactions to quartz-containing and quartz-free chambers.

"About 8% in weight of the original amount of quartz dissolved during the 7-month stay in the chambers, which were freely penetrated by the interstitial fluids; carbohydrates (hexoses and hexosamines) and proteins were adsorbed from these onto the quartz particles.

"It is believed that the results of this experiment are against the possibility that soluble silica (either monomeric or polymerized) is the causative agent of silicosis."

LEVIS, F.; OLIVIERI, A.; CAPPA, P. M.; PERNIS, B.; CARBONARA, A. Studio morfologico della silicosi polmonare come malattia immunitaria. I—Ricerche sperimentali e istochimiche sulla evoluzione delle lesioni da polvere di quarzo puro. [**Morphological Studies on Silicosis as an Immunological Disease. I—Experimental and Histochemical Studies on the Evolution of Lesions induced by Pure Quartz**] [LEVIS, OLIVIERI, CAPPA & PERNIS]. *Med. d. Lavoro.* 1958, Dec., v. 49, No. 12, 735–59, 6 coloured figs. on 2 pls. [Numerous refs.] II. Ricerche sperimentali e istochimiche sulla evoluzione delle lesioni da polveri miste (polvere di miniera di carbone a basso tenore di quarzo.) [**II—Experimental and Histochemical Studies on the Evolution of Lesions induced by Mixed Dusts (Coal Mine Dust with Low Quartz Content)**] [LEVIS, CARBONARA & OLIVIERI]. *Ibid.*, 760–86, 23 figs. [Numerous refs.]

The English summaries appended to the paper are as follows:—

I. "Twenty-two rats were submitted to pure quartz dust inhalation in rotating cages. The study of the induced pulmonary silicotic lesions showed an early stage characterized by quartz phagocytosis by histocytes located in the interstice of the respiratory bronchioles walls. About 45 days after the end of the inhalation, damage to macrophages up to necrosis becomes apparent and a halo of reactive non-phagocytic cells appears, some of which belong to cells of the plasmocytic series.

"The study of cells in the reactive halo around pulmonary silicotic lesions, in the lymphoreticular tissue of interacinar septa and around the bronchi, and in the same tissue of tracheobronchial lymph nodes led to the following conclusions:

"1) during the development of experimental pulmonary silicosis there is constantly plasmocytic reaction at all the examined sites becoming increasingly intense with time;

"2) the reaction of peribronchial and lymph-nodal lymphoreticular tissue appears at a much earlier time than the reaction in the reactive halo around pulmonary silicotic lesions;

"3) the plasmocytic reaction at all examined sites evolves in several stages, i.e. at certain times the reactive halo around pulmonary lesions becomes more marked with a corresponding increase of young elements of the plasmocytic series.

"On the basis of these observations, the importance of the elements of the plasmocytic series is stressed and particularly of the immature ones, as producing antibody globulins. The relationship between appearance of regressive changes of macrophages in pulmonary lesions and the reticulo-histocytic reaction both in pulmonary lesions and in regional lymphoreticular tissue, oriented in a histocytic sense, is pointed out.

"The hypothesis is suggested that from the phagocytes injured by quartz some substances are released that have an immunological activity and are subsequently responsible for the plasmocytic reaction to which the typical hyaline change of silicotic lesions will follow."

II. "After the inhalation of coal mine dust, containing 8% quartz, for a total of 96 hrs. distributed in 30 days, rats show pulmonary silicosis evolving with the typical pattern previously described. After a first stage of dust phagocytosis by histocytes located in respiratory bronchioles interstice, degenerative changes up to necrosis appear in macrophages; then a reactive halo may be observed of non-phagocytic reticulo-histocytic cells, some of which belong to the plasmocytic series. These elements increase with time.

"Some important differences however were observed in comparison with the lesions induced by pure quartz inhalation:

"1) necrosis of macrophages was found to take place much later;

"2) plasmacellular reaction was much less intense.

"These observations have suggested the following hypothesis:

"1) the smaller amount of quartz present in the lesions induces a slow down in the macrophages lesions and therefore a smaller amount of immunologically active material is more slowly released.

"2) The ensuing less intense reaction of reticulo-histocytic tissue with less participation of plasmocytic elements reduces to a minimum the possibility of precipitation of hyaline substance, which is considered, by many Authors, to be the product of antibody globulin precipitation on the site of antigens.

"3) The smaller amount of hyaline substance does not lead to the complete blocking of the lesion as it is observed in silicotic lesions due to pure crystalline quartz inhalation.

"It occurs therefore the paradoxical situation that lesions, being immunologically less active, are more

prolonged in time and of a more continuously granulomatous aspect."

OOTSUKA, S. [**On the Antibodies produced by Subcutaneous Injection of 6 Kinds of Quartz, Japanese Origin**] *Igaku Kenkyu.* Fukuoka. 1958, Oct., v. 28, No. 10, 3479–92, 3 figs. [22 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"The author has noted that subcutaneous injection of quartz particle suspension in rabbits is followed by the appearance of an antibody in the serum of each of the animals. The quartz used was of six kinds, each being of Japanese origin. To describe this result in more detail:—

"(1) 2cc of 2% suspension of quartz particle, when given subcutaneously, at intervals of 4 days, produced in some 60 days an antibody capable of agglutinating the antigen (a serum-covered quartz particle).

"(2) An antibody appearing after subcutaneous administration of one particular kind of quartz was capable of agglutinating that kind of quartz acting as antigen and another kind of quartz acting as antigen as well.

"(3) An absorption test showed that the antibodies produced by injected quartz were divisible into those to be absorbed to any kind of quartz acting as antigen and those to be absorbed only to the injected quartz acting as antigen, namely those common and those specific.

"(4) This fact implies that the proteins adsorbed to the quartz undergo two different kinds of denaturation—denaturation peculiar to the one kind of quartz and denaturation common to the 5 other kinds of quartz.

"(5) The specific antigen, i.e. a layer of protein undergoing the specific denaturation, lies beneath the common antigen, i.e. a layer of protein undergoing the common denaturation.

"(6) There is a small amount of common antibody between an antibody of quartz and an antibody of siliceous stone."

CHVAPIL, M. Der Einfluss von Unterernährung sowie von Diäten verschiedener Zusammensetzung auf die in der Rattenlunge und -leber enthaltene Menge von Skleroproteinen bei experimenteller Silikose. [**The Influence of Nutrition on the Scleroproteins of Rat Lung and Liver in Experimental Silicosis**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1957, v. 15, No. 4, 377–90, 2 figs. [Numerous refs.]

The experiments described were based on the author's and other workers' observation that the rate of collagen formation can be influenced by diet, and on the view of KADLEC (*Výživa lidu,* 1951, v. 6, 135) that a fat-rich diet protects miners against silicosis.

2 experiments were carried out. In the first, 50 mgm. of SiO_2 of 1 micron size (presumably quartz) per rat were injected into 48 rats, keeping a further 30 rats as controls; the animals were kept in 3 groups on a normal, a fat-rich and a low-protein diet. These diets are described in detail. After 3 and after 4·5 months rats were killed, and total collagen and elastin in lungs and livers were determined gravimetrically and by hydroxyproline determination. Both methods gave about the same results. A few histological observations were also made.

In the second experiment, 24 rats were injected each with 25 mgm. of SiO_2, kept on a normal diet for 4 months, and then one group was killed, one was kept on a normal and a third on reduced amounts of the normal diet. 2 months later the experiment was terminated and the same collagen analyses were made as in the first experiment.

Results are given of rat weights, lung weights, and collagen in mgm. and as percent dried tissue with standard deviations which were of the order of 10 to 20%, of the mean values. The main results are also given in 2 graphs.

In the first experiment the silicotic rats had, on a normal diet, 50% more collagen (in mgm.) in their lungs than the controls of equal age, but there was considerably more lung collagen with both the low-protein and high-fat diets. The livers showed no difference due to either diet or dust. In this experiment no typical silicotic lesions were observed but the connective tissue was said to be coarser.

In the second experiment the lung collagen had risen from 15·6 mgm. to 38 mgm. in the quartz-free controls after 6 months; it had risen to 48 and 53 mgm. respectively after 4 and 6 months in the silicotic rats on a normal diet, and the semi-starved rats lost one quarter of their body-weight, but the lung collagen remained at 49 mgm. Liver collagen was slightly lower after semi-starvation.

In a rather long discussion, the author concludes that there is no experimental justification for recommending a diet rich in fat in order to protect workers exposed to silica dust against silicosis.

[This interesting paper is somewhat marred by the apparent lack of silicotic response in the rats injected with quartz. There was apparently only little fibrosis and, on the normal diet, only 10 mgm. extra collagen was due to 50 mgm. of quartz after 3 to 5 months. ENGLEBRECHT *et al.* [this *Bulletin,* 1959, v. 34, 234] found that 25 mgm. of quartz produced *c.* 70 mgm. of extra collagen per rat in the same time interval.]

G. Nagelschmidt

LEVIS, F., OLIVIERI, A. & PERNIS, B. Sul decorso della silicosi polmonare sperimentale in ratti con infezione tubercolare spontanea. [**The Course of Experimental Pulmonary Silicosis in Rats with Spontaneous Tuberculous Infection**] *Med. d. Lavoro.* 1958, Dec., v. 49, No. 12, 725–34, 8 figs. [15 refs.]

The English summary appended to the paper is as follows:—

"The occasional observation of spontaneous tubercular lesions in silicotic rats allowed us to identify some particular changes in the course of experimental pulmonary silicosis. The observation was favoured by the complete independence of localization of tubercular and of silicotic lesions.

"It was found that:

"1) silicotic lesions evolve according to the same pattern observed in the evolution of experimental silicosis due to pure quartz and mixed dusts inhalation;

"2) the onset of the lesions was markedly speeded up and increased; the reticulo-histocytic reaction was much more intense, both locally and regionally and the plasmacellular reaction was particularly evident;

"3) considering the importance of products derived from *Mycobacterium tuberculosis* in enhancing immunological responses, it becomes evident from these observations that the increased severity of silicotuberculosis derives from an increased immunological response of reticulo-histocytic elements;

"4) the silicotic disease, which usually has a multistage course, is therefore changed into a disease with a continuous or subcontinuous course, because of the increased reactivity of reticulo-histiocytic system induced by the presence of tubercular toxins."

Zwi, S. & Becklake, Margaret, R. **Respiratory Function of Witwatersrand Gold-Miners. A Comparison between Radiologically Normal Miners and Control Non-Mining Subjects.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 258–61. [15 refs.]

After many years of underground employment some coal and metalliferous miners complain of disabling dyspnoea, although radiographic examination of the chest shows no evidence of pneumoconiosis. Some observers submit that this pulmonary disability is due to dust inhaled at work [this *Bulletin*, 1956, v. 31, 1233, 1234]. To test this hypothesis lung function studies were made in a random sample of 30 Witwatersrand gold miners whose chest radiographs were adjudged normal. The sample consisted of 3 groups each of 10 subjects in 10-year age-groups between 31 and 60. Each miner had a minimum of 7 years' underground service. A control group of 30 artisans from a railway workshop was chosen from volunteers. These were carefully matched with the miners according to age, physique and socio-economic status. Clinical, radiological, electrocardiographic and haematological examinations were carried out in addition to pulmonary function tests.

No conclusive evidence, clinical or physiological, of an increased respiratory disability among the mining group was obtained, although the average maximum breathing capacity was lower in the miners over the age of 40, but the differences were not statistically significant. *A. Meiklejohn*

Fletcher, G. H. **A Radiological Survey of Miners at Broken Hill.** *Central African J. of Med.* 1958, Nov., v. 4, No. 11, 473–5.

"A report is given of a radiological survey of miners at the Broken Hill mine in Northern Rhodesia. An analysis of the radiological findings made from the survey shows that as a result of employment at the mine, pulmonary fibrosis does occur among the scheduled employees, but that the risk is very low. A long exposure is required before even minimal abnormal radiological changes are discernible.

"Abnormal radiological findings other than pneumoconiosis are also recorded."

[The mine produces lead, zinc and cadmium.]

Sadoul, P., Senault, R., Macinot, C., Aubertin, N. & Guillerm, J. La pneumoconiose des mineurs de fer du bassin de Lorraine. [**Pneumoconiosis in Lorraine Iron Ore Miners**] Reprinted from *Rev. Praticien.* 1958, May 11, v. 8, No. 14, 1505–9, 2 figs.

This is a balanced account of siderosis in the iron-ore miners of Lorraine. The authors review the history, radiological classification, clinical and functional aspects and morbid anatomical features of the condition. An analysis of 575 cases indicates that siderosis occurs only after long exposure to dust, 50% of the cases having had an exposure of over 25 years and less than 5% one of under 15 years. The common association of chronic bronchitis and emphysema, which is poorly related to the X-ray category of pneumoconiosis, is noted and the liability of siderosis to lead to cor pulmonale (though it did so in less than 5% of this series) is mentioned. There appears to be no undue tendency to pulmonary tuberculosis. In conclusion the authors consider that it is illogical to exclude siderosis from the list of compensatable pneumoconioses as is at present the case in France. *I. T. T. Higgins*

Thaer, A. Untersuchungen über die photometrische Auswertung von Konimeterproben. [**Photometric Evaluation of Konimeter Samples**] *Staub.* Düsseldorf. 1958, Nov. 1, v. 18, No. 11, 330–37, 15 figs. [17 refs.]

This article is concerned with the gross evaluation by means of a photocell of the dust deposit impinged upon a konimeter plate without counting or sizing the individual particles.

A konimeter is described and illustrated in which the dust sample is sucked out of a closed sedimentation chamber which is filled 60 seconds beforehand so that the sample contains only dust in the respirable size range and the excessive light extinction due to particles greater than 5 microns is avoided.

The light extinction produced by a sample of dust deposited on a glass plate is defined as the total loss of intensity of a parallel beam after passing through at normal incidence. 2 effects come into play. Firstly, some of the light is actually absorbed in the particles and converted into heat; secondly, the particles deviate some of the light away from its original direction so that it is not recorded by the photocell. Diffraction, refraction and reflection by the particles contribute to the second part of the extinction which is termed light-scattering. Photocell evaluation of konimeter slides can be achieved by measuring either light extinction or the intensity of light scattered by the sample or by a combination of the 2.

Under the normal, bright-field illumination of visual microscopy the specimen is traversed by a cone of light which can be constricted with an iris diaphragm

until it approximates to a parallel beam. As the angle of the illuminating cone is increased and objectives of greater numerical aperture are employed, more and more of the light scattered by the specimen is received to form the visual image. An objective aperture of 0·4 to 0·5 at a magnification of 20 to 25 is necessary to form an accurate image of the dust on a konimeter plate.

Another difficulty in attempting to estimate the number of particles by light extinction is that the reduction in light intensity due to the particles, especially when they are transparent, is very small.

These problems are avoided by measuring the scattered light, as in the Tyndallscope which is employed in the German coal mines to indicate the concentration of dust. There still remains, however, the fact that transparent particles of rock dust scatter much more light than similar sized coal dust so that a knowledge of the fraction of rock dust is required before a reading of the intensity of the scattered light can be translated into dust concentration.

Measurement of scattered light is performed by converting the microscope to dark ground illumination and using a photocell at the eyepiece end. Quite sparse deposits of dust give adequate light intensity but it is necessary to measure and subtract the background illumination. A constant light source is needed and an accumulator was used in the experiments described.

3 types of dark field illumination are described. The system employed utilized a central opaque stop at the entrance to the substage condenser which was large enough just to prevent direct light from entering the objective. A hollow cone of light impinged on the specimen and any scattering towards the optical axis of the microscope contributed to the illumination of the photocell. The acceptance was asymmetrical since light scattered outwards by the particles in the specimen was lost. An advantage of this method of dark-ground illumination is that the light which is scattered through only a small angle is utilized. With dark-ground condensers the angle of the cone of illumination is so wide that a considerable angle of scattering is needed for acceptance.

The other method of illumination discussed uses an annular entrance aperture to the condenser which is imaged on a ring stop at the exit from the objective. This system accepts scattered light symmetrically and at small angles but illuminates the specimen at a much lower level and gives rise to more diffuse background light.

It is suggested that changing the method of illumination might sometimes be useful since the scattered intensity would then depend on size and the proportion of opaque particles in a different way.

Replacement of the opaque central stop by a coloured glass, giving mixed illumination, has previously been tried by the author (*Glückauf*, 1957, v. 93, 647–50).

Measurements of scattered light, with the central opaque stop, were performed with a selenium cell upon the eyepiece. The microscope tube contained 2 polarizing devices one of which could be rotated against an angular scale to extinguish the light reaching the cell. The rotation needed to reduce the cell current to zero gave the relative light intensity which was measured for the whole deposit and also for a clean part of the slide to obtain background scattering. A durable standard "sample" was made by chipping the surface of the plate over an area equal to that of the konimeter's jet by impinging large quartz particles on it. The apparatus is adjusted so that the intensity from the standard sample is always the same amount above background.

Before taking readings on actual dust samples the Vaseline coating of the plate had to be removed. A special irrigation apparatus for this function is described.

Many konimeter samples were counted and measured photo-electrically both before and after ashing so that the intensity of scattered light could be plotted against the number of particles in the 1 to 5 micron size range for rock and for coal. The results showed that these relationships were linear up to a count of 2,500 particles in the sample, which corresponded to about 1,000 particles per cm^3.; rock dust scattered about twice as much light as coal and the spread of the points about the best line was rather greater for rock than for coal.

The author claims that the scattered light is proportional to the area of the particles when they are transparent and to their perimeter or diameter if opaque. This conclusion cannot be accepted in view of the considerably more complicated relationships pertaining for spherical particles which are predicted by the Mie theory of light scattering and have been verified experimentally. It is, however, conceivable that his assumption might have limited validity and thus be of some practical value though he offers no experimental data in support.

Determination of the percentage of rock particles, from photo-electric measurements before and after ashing, is suggested, by means of an empirical formula based upon the author's data, to be possible within 7½%. A considerable saving of time could thus be effected as long as the dust samples continue unchanged as regards the optical properties of the individual particles and the size distribution within the range sampled is not too variable. *C. N. Davies*

LE BOUFFANT, L., with the technical assistance of M. DAVELU. Membranfiltergerät zur Staubprobennahme. **[A Dust Sampling Apparatus using Membrane Filters]** *Staub.* Düsseldorf. 1958, Nov. 1, v. 18, No. 11, 342–3, 4 figs.

The apparatus, which weighs 4·1 kgm., is contained in a leather carrying case measuring 120 × 93 × 237 mm. It comprises a holder for a 20 mm. diameter filter paper through which air is aspirated at speeds up to 500 cc. per minute by a pump driven by a 12 volt battery-operated electric motor. Air from the pump is exhausted through an orifice and the flow is recorded on a dial pressure gauge which measures the pressure drop across the orifice. 20 spare filters are contained in a magazine which is itself exchangeable and is designed to keep the filters clean.

A sampling time of about 10 minutes at 100 to 200 cc. per minute suffices to give a deposit suitable for microscopic counting [see PAULUS, TALVITIE, FRASER &

KEENAN, this *Bulletin*, 1958, v. 33, 51] in average dust concentrations. *C. N. Davies*

CATALDI, R. & ODAGLIA, G. Observations sur la coagulation du sang dans l'intoxication professionnelle aiguë de plomb. [**Observations on Blood Coagulation in Acute Occupational Lead Poisoning**] *Arch. Malad. Professionnelles.* Paris. 1958, Sept.–Oct., v. 19, No. 5, 467–71, 6 figs. [15 refs.]

This is a short paper in which the authors describe the results of examination of the blood coagulability in 13 cases of acute lead poisoning. Reduced coagulability in many industrial poisonings has been reported. As the factors which bring about coagulation of the blood are so numerous it was practically impossible to carry out research into all these factors. The tests which were employed are described in some detail and included tests of coagulation time, the heparin tolerance test *in vivo* and *in vitro* and the heparin activity test. In addition the presence of anticoagulants and also of some of the factors concerned in coagulation were investigated.

The results are recorded graphically and are described. It was found that the coagulability of the blood in these 13 cases was diminished but in general to only a slight extent. The most important but not the only factors involved in this reduction were a lowered activity of prothrombin and of factor VII.

M. E. Delafield

ALBAHARY, C., TRUHAUT, R. & BOUDÈNE, C. Imprégnation plombique; épreuve de plomburie provoquée par aérosol de versenate de calcium disodique. Possibilité d'une prophylaxie. A propos d'une enquête dans une entreprise d'accumulateurs. [**Test for Urinary Lead Excretion Induced by an Aerosol of $CaNa_2EDTA$. Possibility of Prophylactic Use**] *Arch. Malad. Professionnelles.* Paris. 1958, Sept.–Oct., v. 19, No. 5, 485–7.

In this short paper the authors give some account of conditions in an accumulator factory where ventilation was unsatisfactory and considerable amounts of lead dust were found in the atmosphere at different points. In an examination of 13 of the workers it was found that 11 of these had various degrees of punctate basophilia. A special investigation was made of 6 of these men who volunteered for the study of the effect of the inhalation of an aerosol of $CaNa_2EDTA$ on their urinary excretion. The findings are set out in a table which gives numerical data of the blood and urinary lead content before and after the aerosol treatment. The aerosol treatment was repeated 2 months later. It was found that the aerosol treatment on the first occasion increased the urinary lead excretion from 3- to 30-fold and that the second treatment was followed by similar though not identical increases.

In the discussion it is suggested that although inhalation of $CaNa_2EDTA$ is not a suitable method of therapy in plumbism it might be of value as a prophylactic for workers exposed to lead risk. The small amounts of the versenate inhaled are not likely to cause any trouble, but the possibility that prolonged administration might result in undue elimination of metallic ions other than lead is realized. *M. E. Delafield*

PERYASSÚ, D., NEGREIROS, E. B. & DE CARVALHO, L. P. Cromonecrose e dermatoses similares (botao de cromo). [**Chrome Necroses and Similar Dermatoses (chrome button)**] *Rev. Assoc. Méd. Minas Gerais.* 1957, Sept.–Dec., v. 8, Nos. 3/4, 169–74, 7 figs.

The authors point out that chrome and its derivatives cause lesions of 2 different types, acting as: (a) primary caustic irritants, and (b) as allergens. Chrome necroses affect the parts of the body exposed at work and are most evident in those who sweat a great deal.

Clinically the lesions appear as erythematous or papular rounded or oval foci on the skin, varying from 3 mm. to 1 cm. in diameter. Later these lesions rapidly become crateriform ulcers with raised walls surrounded by inflammatory haloes. In some cases the ulcer can penetrate down to the bone. In the authors' patients patch testing with 0·5% potassium bichromate was negative, and this, although there was some hypersensitivity, almost excludes an allergic origin. They give details of 5 patients in whom biopsy of the lesions was performed; when tested with 0·5% bichromate only 1 was positive. *W. K. Dunscombe*

SANTIAGO DE OLIVEIRA, E. Cromismo. [**Chromism.**] *Rev. Assoc. Méd. Minas Gerais.* 1957, Sept.–Dec., v. 8, Nos. 3/4, 223–37, 11 figs.

Among the industries using chrome and its derivatives the author mentions especially the preparation of basic chrome sulphate as particularly likely to cause trouble. As 2 cases of chrome ulcer were unexpectedly notified, an investigation of the factory was made with examination of 27 workers. 21 were found to have perforation of the nasal septum and 2 of these had ulcers on the skin as well. No cases of otitis media or externa, or of keratitis, were seen.

The factory was located in the environs of São Paulo and produced basic chrome sulphate for preparing chrome leather. The basic sulphate was produced in the factory from the raw material chromite by appropriate processes—crushing, bolting, etc.—until finally a fine green powder, the basic chrome sulphate, was produced. Hygiene in the factory was non-existent either for the individual workers or generally; the atmosphere was very dusty, and dust lay thick on the walls and floors.

The patients had complained of nasal congestion, sneezing, pain, rhinitis, coryza and haemorrhages even up to frank epistaxis, and once the mucosa was destroyed the cartilage was rapidly perforated. The ulcer was almost always sited at the anterior lower part of the septum, in the area where the orifice leading to the tube of Ruysch is situated. In this site the powder can collect and is sheltered from the normal processes of elimination and so its noxious action is relatively undisturbed. Lateral X-ray of the noses of

the patients showed clearly the coincidence of the site of perforation and of the above-mentioned orifice. Pain was a constant feature and the minimum time taken for perforation to occur was 2 months. 1 of the 6 persons who showed no lesions had worked in the most dusty site in the factory for 2 years. The general state of the patients was not affected and no pulmonary lesions were found.

The author makes extensive recommendations as regards general and individual preventive measures including the weekly examination of employees, those with rhinitis or skin erosions being put temporarily off work. He discusses also the question of sick benefit and compensation in the light of existing legislation which does not cover chrome ulceration at any site.

W. K. Dunscombe

WEST, B. & SUNDERMAN, F. W. **Nickel Poisoning. VI. A Note concerning the Ineffectiveness of Edathamil Calcium-Disodium (Calcium Disodium Ethylenediaminetetraacetic Acid).** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 480–82. [13 refs.]

Edathamil ($CaNa_2EDTA$) has been reported as useful in poisoning by various metals and as an antidote for nickel chloride intravenously in rabbits [this *Bulletin*, 1956, v. 31, 926]. It forms stable chelates with many metals, including nickel. Its LD50 value is 500 to 700 mgm./kgm. depending on species and route. When administered parenterally it is rapidly excreted in the urine. In nickel carbonyl poisoning in mice and rabbits the authors showed that edathamil was ineffective in doses up to 500 mgm./kgm. After exposure to nickel carbonyl at a concentration of 0·06 mgm. per litre for 30 minutes, mortality ratios of the mice in the groups receiving various amounts of edathamil did not differ significantly from those untreated, and no significant differences were found in the distribution of nickel in lungs, kidney and liver. 7 rabbits were exposed for 30 minutes to nickel carbonyl, 2 or 1·75 mgm. per litre. All died within 90 hours whether untreated or given edathamil intravenously at a dose of 500 mgm./kgm. or an additional 250 mgm./kgm. 18 or 4 hours later. Distribution of nickel in vital organs and, in one pair, the amount of nickel in 24-hour collections of urine, were essentially similar. Intraperitoneal administration of a solution of nickel nitrate, 0·01% (w/v) in doses of 0·5–2·5 mgm./kgm. to mice, and of a similar 0·1% solution of 1 mgm./kgm. to rats, was followed in 15 minutes by edathamil intraperitoneally, but no protection resulted. Mortality ratios showed that edathamil was ineffective as an antidote for a lethal injection of an inorganic nickel salt.

M. Patricia Fitzsimons

ROSCHTSCHIN, I. V. Das Vanadium als industrielles Gift. [**Vanadium as an Industrial Poison**] *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 4, 492–501. [11 refs.]

This paper contains a clear, informative account of the industrial hazards of exposure to vanadium which is based on the literature and the author's experience. Vanadium which is present as salts and oxide in the earth's crust in an estimated concentration of 0·016%, *i.e.* higher than those of lead, zinc and antimony, is not found in deposits but in minute amounts in other minerals, in water and in plants and animals including man. It is being used to an increasing extent in a variety of industrial processes and hence its toxicity to man is becoming more important.

In industry the metal may contaminate the atmosphere as finely divided dust, vapour or aerosol of vanadium pentoxide; sodium, ammonium and calcium vanadate or ferrovanadate (an alloy of iron and vanadium). Sections of the paper deal with the working conditions in factories where vanadium is used, the toxic effects of vanadium on workers, toxicity studies in experimental animals and the prevention of vanadium poisoning.

Observations in industrial workers and in the animal experiments show that the main toxic effects of vanadium are (1) its irritant action which causes hypersecretion from mucous membranes, salivation, lachrymation, sneezing, cough and vomiting, and (2) its action on the vascular system in causing stasis in the capillaries, perivascular swelling and local haemorrhages. There may also be bronchial spasms or bronchitis of asthmatic character. Vanadium is absorbed from the lungs into the blood and may cause toxic effects in the heart, nervous system and the general metabolism. Excretion of vanadium, which is slow, is by urine, faeces, bile, bronchial secretion, tears and saliva.

The most toxic of the vanadium compounds is the pentoxide and the least harmful is ferrovanadate. It is recommended that the concentration of vanadium in industrial atmospheres should not exceed 0·0001 mgm. per litre of air.

M. E. Delafield

RICHESON, Edna M. **Industrial Thallium Intoxication.** *Indust. Med. & Surgery.* Miami. 1958, Dec., v. 27, No. 12, 607–19. [41 refs.]

"An extensive search of the literature available prior to 1934 revealed 778 cases of human toxication with 46 deaths." Most of these cases of thallium poisoning (692) and 31 of the deaths resulted from the clinical use of thallium salts mainly as a depilatory.

In this paper there is a review of the literature on industrial thallium poisoning which introduces an account of the study of the health of workers engaged in a factory in Ohio where diamonds are separated from other minerals by gravity in varying concentrations of solutions of organic thallium salts. There is a report of considerable length on the clinical findings in the 15 men engaged in this work of whom 12 "had complaints which could have stemmed from their thallium exposure". Tables set out particulars of age of workers, time interval between engagement and first complaints, nature and frequency of symptoms, blood pressure, differential blood counts and amounts of thallium found in the urine. Recommendations are made for the prevention of occupational thallium poisoning.

A diagnosis of thallium poisoning was made eventually in 6 of these workers. Some stress is laid on the difficulties of diagnosing the intoxication. The chief

complaints were abdominal pain, fatigue, loss in weight, pain in the legs and nervous irritability. Appendicitis was diagnosed originally in 3 of the men and 2 of them were operated on. Albuminuria, haematuria, abnormal liver function tests, increase in glucose and protein in the cerebrospinal fluid and increased blood pressure were also noted in some of the men.

M. E. Delafield

GUYOTJEANNIN, C. & VAN STEENKISTE, J., with the technical collaboration of G. VALLÉE, J. LE LAY & A. PAULIN. Action du trichloréthylène sur les protéines et les lipides sériques. Étude chez 18 ouvriers travaillant en atmosphère polluée. **[Action of Trichlorethylene on Serum Proteins and Lipids. Study in 18 Subjects Working in a Polluted Atmosphere]** *Arch. Malad. Professionnelles.* Paris. 1958, Sept.–Oct., v. 19, No. 5, 489–94.

The literature on the toxicity of trichlorethylene has been concerned more with acute than with chronic poisoning. The work described in this paper consisted of chemical examinations of the blood sera of 18 workers who had been exposed to an atmosphere polluted with trichlorethylene vapour, for periods of months or years, in order to study the possible effect of the solvent on the liver.

The methods employed to examine the sera are described in some detail and the numerical results of the analyses are set out in 2 tables. The chief tests were flocculation tests of liver function, electrophoretic analysis of protein fractions, total lipid content, analysis of lipid fractions and unsaturated fatty acid content.

It was found that the liver function tests mostly gave normal results and only rarely weak positives. A fairly marked increase in the β-globulin fraction was demonstrated. Various departures from the normal in the amounts of total lipids and lipid fractions were noted frequently, which points to disturbances of lipid metabolism in these workers exposed to trichlorethylene.

M. E. Delafield

PHAIR, J. J., SHEPHARD, R. J., CAREY, G. C. R. & THOMSON, M. L. **The Estimation of Gaseous Acid in Domestic Premises.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 283–92, 6 figs. [19 refs.]

"A description is given of a small sequence sampler that gives six-hourly readings of gaseous acid concentration in domestic premises. Samples are returned to the laboratory for analysis by the conductivity method. Factors affecting the rate of sampling and evaporation of absorbent solution are critically evaluated. Evaporation is an important problem with the original model and methods of minimizing water loss have been incorporated in later designs of the apparatus. Gaseous acid measurements largely reflect the amount of SO_2 in a suburban atmosphere and an efficiency of 95% can be obtained with single-stage sampling. Ammonia and hydrochloric acid vapour are also absorbed although these are present in lesser and approximately equal amounts. Sulphur trioxide is not absorbed to any significant extent, but this is a minor constituent of suburban atmospheres.

"The variation between different sampling units in the same room is considerable in the presence of dry gaseous SO_3, and even under normal room conditions the 95% confidence limits of observations made from a single point are $\pm$ 0·0024 p.p.m. Differences between different parts of a large building are even greater. Indoor measurements show a general tendency to follow outdoor readings with a lag of up to two hours; however, the indoor concentrations of gaseous acid are on the average much lower, and do not show the sharp peaks seen at outside locations. The relationship between gaseous acid levels in different parts of the city is not constant since in each area the industrial output is supplemented by a seasonally varying domestic heating load. The relationship between gaseous acid and particulate contaminants also varies in different parts of the town, perhaps on account of differing amounts of alkaline pollutants in the atmosphere."

[This is a valuable contribution, and interested readers should consult the original for full details concerning sampling apparatus and methods.] *P. J. R. Challen*

EFFENBERGER, E. Gefährdung der Beamten des Paskontroll- und Zolldienstes an Grenzübergängen durch Auspuffgase. **[Danger to Passport and Customs Officers from Exhaust Gases]** *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 403–21, 11 figs. [20 refs.]

The elaborate study described in this paper was undertaken because passport and customs officers had complained of symptoms at rush hours which they attributed to exhaust gases from the running engines of stationary motor vehicles. Sections of the paper deal with: (1) the toxic constituents of exhausts from petrol and Diesel engines which include carbon monoxide, nitrous gases and aldehydes; a description from the literature of the clinical effects of these and of lead dust from ethyl fluid is given, (2) the movement of exhaust gases under different meteorological conditions, (3) the symptoms complained of by officers at 2 frontier stations between Germany and Switzerland; a long list of complaints of the officers and their frequency is given and the most important were headache (48%), a feeling of oppression in the gastric region (8%) and irritation of the throat (8%), (4) the traffic concentration at different periods, (5) measurement of the carbon monoxide concentration in the air, (6) the association of traffic concentration and carbon monoxide content; this was examined at length by statistical methods, (7) statistical examination of the relation between the frequency of symptoms and the traffic concentration and also the velocity of the wind and (8) the carbon monoxide content of the blood of the officers, which was found to increase during work periods.

From the results of the study there is considered to be no doubt that the officers at these 2 frontiers are endangered by exhaust gases at times of heavy traffic and when the air is still. Some recommendations are made for lessening this danger which arises not only from carbon monoxide but also from other constituents of the exhaust. *M. E. Delafield*

BIONDI, S. Sull'artigianato in rapporto all'automobilismo. **[The Artisan's Work in relation to Automobilism]** *Rass. Med. Indust.* Rome. 1958, Nov.–Dec., v. 27, No. 6, 579–97, 13 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"A description is given of the work performed by engineers, coach-makers, electricians and tyre-makers in the motor-car industry, as well as by petrol-pump personnel.

"These artisans are exposed to various types of poisoning, such as by Pb tetraethyl, by CO, solvents and nitrate compounds.

"Moreover, they are often compelled to work in uncomfortable or tiring positions and petrol-pump personnel are subject to perfrigerating factors.

"Clinical examination, however, showed only a considerable frequency in respiratory diseases among petrol-pump personnel."

GALLO, G. & GHIRINGHELLI, L. Patologia professionale da esametilendiamina. **[Occupational Disease due to Hexamethylendiamine]** *Med. d. Lavoro.* 1958, Nov., v. 49, No. 11, 683–9, 1 fig.

The English summary appended to the paper is as follows:—

"Hexamethylendiamine concentration in the air was determined in a plant for the synthesis of this compound for hydrogenation of adipic nitryl and in a plant of production of the same compound for hydrolysis of nylon shreds. In normal conditions the observed values were 2 mg/mc in the first plant and 5.5 mg/mc in the second plant. During autoclave discharging in the adipic nitryl hydrogenation plant and during autoclave filling in the shreds hydrolysis plant, the average concentrations were 32.7 mg/mc and 131.5 mg/mc respectively.

"20 workers from these plants were examined: 8 showed a moderate irritation of the conjunctivae and the upper respiratory tract; 7 complained of dyspeptic trouble. One worker suffered of acute hepatitis followed by an eczema due to hypersensitivity to hexamethylendiamine, while conjunctival and upper respiratory tract irritation was attributed to hexamethylendiamine inhalation; dyspeptic disorders were attributed to irregularity of meals due to shift work.

"Blood test and other laboratory tests on the mentioned 20 workers gave normal results. It is concluded that hexamethylendiamine, although highly caustic, has a low toxicity because its vapours are rapidly neutralized by CO_2 of the air, with formation of hexamethylendiamine carbamate, a stable non-irritating salt."

DEICHMANN, W. B., RADOMSKI, J. L., MACDONALD, W. E., KASCHT, R. L. & ERDMANN, R. L. **The Chronic Toxicity of Octadecylamine.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 483–7.

Commercial octadecylamine (containing 20% hexadecylamine) may be added at a rate of 2·5 p.p.m. as an anti-corrosive to steam used to cook food, and the maximum concentration expected in the food varies from 0·25 to 0·5 p.p.m. Chronic toxicity studies for 2 years in rats fed with a diet containing octadecylamine up to 500 p.p.m. showed no changes in weight, blood counts, mortality distribution, food consumption or micropathology. In dogs given octadecylamine at levels of 0·6 or 3 mgm./kgm., the latter equivalent to 100 p.p.m., daily for 5 days each week for a year, no toxic effects were observed, but in 3 given 15 mgm./kgm. slight changes (weight and pale-staining intestinal villi) and one death from gastro-intestinal irritation suggested some toxic effect.

The subacute toxicity in rats was compared with that of stearic acid, a compound with a similar carbon skeleton. In this preliminary experiment the amine and the acid, each fed at a level of 3,000 p.p.m. for 209 days, gave similar toxic reactions, anorexia and increased mortality rates, the mean survival period on the amine being less than on the acid but the mortality ratio for the acid being the greater. Rats fed stearic acid showed severe pulmonary infection and abundant iron-containing pigment in the spleen. Rats fed octadecylamine also showed varying degrees of pulmonary infection but also intestinal and mesenteric lymph node lesions, and some had focal granulomas in the liver. The mucosa of the small intestine contained a diffuse aggregation of foamy histiocytes, not stained with Sudan IV. The enlarged matted lymph nodes showed a marked granulomatous reaction with histiocytes, nodule formation, necrosis and fibrosis. Maximum non-toxic levels of octadecylamine appear to be 500 p.p.m. for the rat and 100 p.p.m. for the dog.

M. Patricia Fitzsimons

TROLL, W. & NELSON, N. **Studies on Aromatic Amines. I. Preliminary Observations on Benzidine Metabolism.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 499–503, 3 figs. [11 refs.]

KINOSIAN, J. R. & HUBBARD, B. R. **Nitrogen Dioxide Indicator.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 453–60, 6 figs. [10 refs.]

"A rapid, simple, and convenient semiquantitative method for the determination of NO_2 in air has been developed. The method does not appear to be susceptible to interference from nitric oxide (NO) or other gases commonly found in industry.

"The method as presented will determine NO_2 concentrations in the range of from 1 to 50 ppm with an accuracy of $\pm 50\%$, but with further refinements the accuracy can be increased. By sampling larger volumes of air, concentrations of NO_2 less than 1 ppm can be determined."

HILL, W. H., MERRILL, Jean M. & PALM, Betty J. **Direct Determination of Boranes by the Carmine Method.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 461–3.

DEICHMANN, W. B., MACDONALD, W. M., COPLAN, M. M., WOODS, F. M. & ANDERSON, W. A. D. **Para Nitrobiphenyl, a New Bladder Carcinogen in the Dog.** *Indust. Med. & Surgery.* Miami. 1958, Dec., v. 27, No. 12, 634–7, 4 figs.

In the manufacture of para-aminodiphenyl or "para aminobiphenyl (PAB) (Xenylamine)" an intermediate compound para-nitrodiphenyl or "para nitrobiphenyl (PNB)" is used. The carcinogenicity of both these compounds has been reported and the manufacture of PAB was discontinued. The study reported in this paper was undertaken to discover whether the bladder tumours "noted in men exposed to Xenylamine may have been partially due to PNB" remaining as an impurity.

Purified PNB in a dose of 0·3 gm. in capsule was administered 3 times a week to 4 young adult female mongrel dogs which were examined by cystoscope at intervals of 5 or 6 months. In 3 of these animals bladder tumours were seen after from 25 to 33 months. These animals were killed and the gross and microscopical appearances of the bladder tumours are described with photographs. In the fourth animal no bladder tumour was seen.

"In these experiments with dogs, PNB appeared to be as potent a carcinogen as para aminobiphenyl (PAB) (Xenylamine)."

[See also this *Bulletin*, 1958, v. 33, 583.]

M. E. Delafield

GHIRINGHELLI, L. & SIRONI, G. Dimetilsolfato e catalasi. [**Dimethylsulphate and Catalase**] *Med. d. Lavoro.* 1958, Nov., v. 49, No. 11, 690–93. English summary (8 lines).

In experiments aimed at trying to ascertain in what way dimethyl sulphate (DMS) exerts its toxic action, the authors studied its effect on the blood catalase in 5 guineapigs which were exposed to a concentration of 75 p.p.m. (*i.e.* only slightly less than the LD50) for 20 minutes in an 8-litre box through which air was pumped at the rate of 85 litres per hour. Blood was taken from the animals before the test and at various intervals afterwards.

The results showed that dimethyl sulphate does not inhibit the activity of blood catalase.

In a second series of experiments a constant quantity of crystallized catalase was tested against a varying amount of dimethyl sulphate. Here even in heavy doses catalase activity was not inhibited, nor was the absorption spectrum altered. *W. K. Dunscombe*

GHIRINGHELLI, L. & BARTALINI, E. Attività catalasica e formazione dei corpuscoli di Heinz. [**Catalase Activity and Heinz Body Formation**] *Med. d. Lavoro.* 1958, Nov., v. 49, No. 11, 694–7, 1 graph. English summary.

The catalase activity of blood samples and Heinz-body formation were tested *in vitro* with 2–4 dichlorophenol (2–4 D), and in addition the activity of crystallized catalase was tested with varying amounts of the same chemical.

2–4 D was selected for Heinz-body formation because others had already shown that even in concentrations of 10^{-6}M it was able to inhibit crystallized catalase and cause Heinz-body formation.

Citrated guineapigs' blood was used and the results showed that even in concentrations strong enough to cause the formation of Heinz bodies and even to destroy the red cells, catalase activity was not inhibited. However, in a concentration of 10^{-6}M the activity of crystallized catalase was considerably lessened and almost totally inhibited in a concentration of 10^{-2}M.

The authors conclude that with 2–4 D the formation of Heinz bodies is not associated with inhibition of catalase, and that blood catalase contains some substance capable of neutralizing the anti-catalase activity of 2–4 D. *W. K. Dunscombe*

JOFFE, M. H., GONGWER, L. E. & PUNTE, C. L. **Studies on the Acute and Subacute Toxicity of Bis(2-Ethylhexyl) Hydrogen Phosphite.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 464–9.

Bis(2-ethylhexyl) hydrogen phosphite, a liquid insoluble in water, with a low vapour pressure, boils at 163°C./3 mm.Hg. Care is needed in handling because of the insidious intoxication in the animals and skin reaction. Intragastric administration to rabbits and feeding to guineapigs seemed innocuous, and also ocular administration to rabbits except for temporary conjunctivitis and necrosis of the palpebral mucosa. Inhalation for ½ to 4 hours of high mist concentrations gave rats temporary respiratory distress (no deaths and no significant post-mortem lesions) but gave guineapigs greater distress, and in those that died pulmonary oedema and necrosis of bronchial epithelium and gastric mucosa. Guineapigs exposed for 6 hours, 5 days a week for 10 weeks, to saturated vapour survived (no signs before or after killing), and to saturated vapour plus mist, nearly all survived (respiratory tract irritation). On intraperitoneal injection the LD50 values in mice, rats and guineapigs were 0·62, 1·5 and 0·7 ml./kgm. In rabbits the LD50 for intravenous administration was calculated to be 0·1 ml./kgm. for an observation period of 24 hours; they died of lung haemorrhage and oedema. No evidence of inhibition of cholinesterase activity in rabbits and dogs given 0·02 ml./kgm. intravenously could be demonstrated.

Cutaneous administration to clipped backs of rabbits gave results almost equivalent to intraperitoneal injection and only separated from the intravenous toxicity by a 1 to 10 ratio. Single skin doses of 1 ml./kgm. killed 3 of 4 animals in 5 days and 2 ml./kgm. killed all 4 within 2 days. Clothing with twill treated with 4 ml./kgm. produced about a 4-fold protection, 50% mortality in 5 days. Before death the only signs were posterior paralysis, prostration, anorexia and lassitude. The skin had parchment-like areas of coagulative necrosis and one-half the animals showed stomach ulceration. A daily application of 0·07 ml./kgm. repeated 18 times, whether to the same or different areas, though not lethal, produced erythema and necrosis.

The most probable human contamination is percutaneous. Several persons during these experiments developed dermatitis with signs similar to those of the rabbits, with every indication that the phosphite was the agent. Inhalation does not appear a likely means of intoxication. *M. Patricia Fitzsimons*

DUBOIS, K. P. **Potentiation of the Toxicity of Insecticidal Organic Phosphates.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 488–96. [10 refs.]

In this long article are described studies by the author and others to elucidate possible hazards from ingestion of foods contaminated with more than 1 of the 9 investigated organic phosphorus insecticides permitted on food crops. Permissible levels were based on additive effects and until recently no evidence of potentiation existed. Less-than-additive effects noted with some pairs, when given simultaneously, each having similar mechanisms of action, showed that the time of maximal depression of cholinesterase varies, and imply possible additive toxicity if the doses are spaced so that maximal effects occur simultaneously. 3 combinations of 15 pairs of compounds resulted in potentiation of acute toxicity in rats, and 1, EPN plus malathion, in potentiation subacutely in dogs fed simultaneously with safe levels of each. Acute or subacute toxicity tests cannot explain the mechanism of potentiation. Studies with ethyl p-nitrophenyl thionobenzenephosphonate (EPN) and malathion (o,o-dimethyl dithiophosphate of diethyl mercaptosuccinate) eliminated 2 possible mechanisms, and indicated that the effect occurs when one interferes with the enzymatic detoxification of the other by inhibiting an esterase in liver, serum and other tissues. This non-specific esterase hydrolyses the toxic oxygen analogue. Interference with the detoxification of compounds such as malathion, whose low mammalian toxicity depends upon efficient detoxification, markedly increases toxicity. Methods recently developed showed *e.g.*, that the liver and serum of rats fed for 2 weeks with 5 p.p.m. EPN caused 28·6% and 39·5% inhibition of the detoxification of malathion. Results, more sensitive than those from tests based on cholinesterase inhibition, provide an explanation for the potentiating effect of EPN and illustrate the value of subacute tests in considering hazards caused by potentiation. Agents such as EPN may be of value in research in normal metabolism. Acute exposure to certain combinations of organic phosphates on the same or successive days should be avoided in manufacture and use. *M. Patricia Fitzsimons*

HARGER, R. N. & SPOLYAR, L. W. **Toxicity of Phosphine, with a Possible Fatality from this Poison.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 497–504, 3 figs. [18 refs.]

The fatal concentration of phosphine may be 5 to 10 p.p.m. if breathed 2 to 4 hours daily, and the effect may be cumulative. A review of the 59 cases of phosphine poisoning published included 3 (2 fatal) in welders who breathed acetylene from portable generators. Calcium carbide contains small amounts of calcium phosphide. Symptoms included fainting, and autopsies frequently showed pulmonary oedema. The authors found no reported death or illness of operators of acetylene generators from inhaling acetylene but their investigations suggest a death in such a plant from inhaling phosphine gas, possibly contributed to by acetylene during a fainting attack. An acetylene generator operator, aged 16, of good physique, was found unconscious and pulseless with his face partly over an open hopper filled with carbide; the generator tank below was partly refilled with water and the valve between not entirely closed. He had been running 2 generators for 6 weeks and after 3 weeks had reported dizziness and unconsciousness; 10 days before death he had become unconscious while driving but although the car overturned had only had a bruised cheek. Autopsy showed only acute pulmonary oedema, blood-tinged.

While the tank is refilling with water to 21 in. from the top, the operator recharges the hopper with carbide from one or two 600 lb. drums, displacing 8 cu.ft. of hopper gas, taking 4 to 8 minutes, and then screws the cover. Analyses of gas in the hopper and tank, and of the air above the hopper during recharging gave an estimate of the operator's exposure, *i.e.* acetylene 2% to 12%; phosphine, depending on variables, probably 8 p.p.m. for 1 to 2 hours daily; and for short periods hydrogen sulphide less than 10 p.p.m. and arsine less than 0·3 p.p.m. *M. Patricia Fitzsimons*

PETTY, C. S. **Histochemical Proof of Organic Phosphate Poisoning.** *Arch. Pathology.* 1958, Oct., v. 66, No. 4, 458–63, 6 figs. [12 refs.]

" Histochemical demonstration of diminished cholinesterase activity in the motor end-plate region in intercostal muscle from a case of fatal human poisoning with Systox, a toxic organic phosphate preparation, was the method used to prove the cause of death. This was correlated with the postmortem red blood cell cholinesterase level. In vitro studies with human muscle and both in vitro and in vivo studies of rat muscle demonstrate that Systox is capable of depressing the cholinesterase at motor end-plates."

SAMITZ, M. H. & POMERANTZ, H. **Studies of the Effects on the Skin of Nickel and Chromium Salts.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 473–9.

The skin of guineapigs was not irritated by 0·5% $K_2Cr_2O_7$, 4% $NiSO_4$ nor by 1% sodium lauryl sulphate; but preparation of the skin by the last, or its addition to the first 2 salts, rendered them capable of producing a reaction; but not, in these experiments, one resulting in allergy.

Patch tests in human subjects, known to be allergic to chrome or nickel, were positive at much higher dilutions when sodium lauryl sulphate took part in the reaction.

Attempts to inhibit cutaneous reactions to chrome by protection of the SH groups with formalin, cysteine or glutathione or by means of chelating agents, ascorbic acid, etc., were only partially successful. But in the case of nickel, ointments of EDTA, sodium diethyldithiocarbamate (which has been successfully employed against $Ni(CO)_4$) and dimethyl glyoxime all inhibited the reaction and the authors have done some work to show how long can elapse between exposure and treatment, etc.

Dimethylglyoxime gives a pink colour-reaction with salts of nickel and it is here used to make a rough estimate of the amount of nickel leached out of coins, etc., by sweat. The authors hint that domestic availability of detergents may account for the sudden increase of nickel allergy in women. [They do not comment, however, on the fact that nickel allergy with or without eczema of the hands is rare in males, all of whom carry nickel objects in their trouser pockets, sweated into by both hands and thigh, washed with detergents or perhaps never washed at all during the lifetime of the suit.]

That some of the guineapigs used in the experiment absorbed chrome but not nickel was shown by spectrographic analysis of certain organs but since the animals were not isolated it might well have been ingested rather than absorbed through the skin. Chrome was not detected either in the blood or in the reacting skin of chrome-allergic patients. *J. H. Twiston Davies*

Peryassú, D., Negreiros, E. B. & De Carvalho, L. P. Epidermodermite profissional dos manipuladores de cimento e sensibilização ao bicromato. [**Occupational Dermatitis of Cement Workers and Sensitivity to Bichromate**] *Rev. Assoc. Méd. Minas Gerais.* 1957, Sept.–Dec., v. 8, Nos. 3/4, 217–21, 3 figs.

Cases of dermatitis in cement workers were investigated. The condition was a vesicular dermatitis of rather multifarious aspect affecting especially the hands, forearms, dorsa of the feet, legs and knees, which regressed if the patient stopped handling cement. 30 cases of occupational dermatitis which had been classified as dermatitis vesiculosa were studied. 14 patients were masons, 6 were plasterers, and all the rest had had to work with cement at times. All were patch-tested with 0·5% bichromate and also with 10% lime and with some local varieties of cement, and re-exposure tests were made on 19 who returned to work. The results were (a) 29 positive to bichromate; (b) 25 positive to cement. The patients' ages varied from 22 to 66 years, the length of time in their present occupation from 2 to 40 years, and the onset of the disease varied from 20 days to 20 years after starting work. 17 of the 19 re-exposure cases showed frank intolerance with rapid reappearance of symptoms. White persons were more susceptible than those with more coloured skins, and the incidence was independent of age and length of time at work.

The authors conclude that masons' eczema is an allergic condition, but there is some hypersensitivity to bichromate. The race factor is important.

W. K. Dunscombe

World Health Organization. Technical Report Ser. No. 154. **Post-Graduate Training in the Public Health Aspects of Nuclear Energy.** Fourth Report of the Expert Committee on Professional and Technical Education of Medical and Auxiliary Personnel, Geneva, 23–28 September 1957. 53 pp. 1958. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

No one concerned with public health can afford to miss this brochure of 53 pages, packed with vital information on the menace that ionizing radiation can be unless protective measures are systematically used.

On p. 7 we read: "The extent to which atomic energy . . . may present a public health problem in any particular country depends on that country's stage of development in this field . . . If it should deem its requirements to include training in nuclear energy for its public health personnel, then it may consider taking some of the steps outlined in this report". Our own country is in the forefront of exploiting nuclear energy and it is certain that the expert information in this report will be widely acceptable. We may quote again a highly significant statement: "While the problems of radiation exposure have many close similarities to those of industrial toxicology generally, there are important differences. No chemical industry has been demonstrated to be potentially capable of causing such lasting injury to an entire population as compared with that which might occur from a large reactor or processing plant. There is no other human activity utilizing forces which are comparable in their power to change permanently the genetic structure of living things".

In the event of a major breakdown in a reactor the duties of the industrial personnel would be very complex and close collaboration with health physicists and other nuclear scientists would be essential.

The authors of this report see that inevitably there will be a demand for legislation to put into effect what are at present recommendations and in framing a suitable legislative act which would empower a governmental agency to adopt rules and regulations, the code outlined here would certainly be of great service since there is hardly a single aspect of hazard that is not considered, often in great detail.

The whole drafting of this report is so concisely expert that an adequate abstract of its contents would rival in length the report itself. The report is of the greatest interest and highest importance. *S. Russ*

Shinn, D. H. **Health Hazards from Powerful Radio Transmissions.** [Correspondence.] *Nature.* 1958, Dec. 27, v. 182, 1792–3, 1 fig.

Since the early days of radar there has been an awareness of the possible danger of the radiation to the health of operators, but it is significant that the outstanding effect is one of heat generation and not biological as is the case with the ionizing radiations. The article in question is concerned with the heating effects which can be dangerous at considerable distances from the transmitter. The heating depends not only on the

power of the latter but upon the wave-length of the radiation emitted. It is stated on the authority of SCHWAN and LI (1956) that the maximum steady flux tolerated by the body is 30 mW/cm.^{2} for frequencies less than 500 Mc./s.; 10 mW/cm.^{2} for frequencies between 1000 Mc./s. and 3000 Mc./s. and 20 mW/cm.^{2} for higher frequencies.

The author is mainly concerned with the design and siting of powerful transmitters with a view to reducing the thermal hazards.

Reference is made in the text to "*Proceedings of a Symposium on the Physiological Effects of Microwaves*" in *Trans. Inst. Radio. Eng., PGME—4* (1956).

S. Russ

KLIMKOVÁ-DEUTSCHOVÁ, Eliška & ODVÁRKOVÁ, Jitka. Messungen elektrocutaner Leitungskurven bei Werktätigen unter Einwirkung ionisierender Strahlen. [**Measurement of Electrical Conductivity in the Skin of Operatives Exposed to Ionizing Rays**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 2, 178–83, 4 figs. [10 refs.]

A dryness of the skin of the hands has been observed among radio-diagnosticians which has been attributed to the small doses of X-rays received in the course of manipulations despite the usual precautions for safety.

The authors have undertaken measurements of the electrical conductivity of the hands of those so affected. The method consists of applying a constant e.m.f. of about 12 volts to 2 electrodes, one in the palm, the other on the back of the hand. The resulting current is registered graphically and is maintained for a considerable time (hours) but for exactly how long cannot be determined from an inspection of the graphs, which are singularly devoid of descriptive terms. The graphs were obtained experimentally from various groups of people but those of chief interest were the radio-diagnosticians and their controls. The authors maintain that their differences are quite significant and not only is this the case between controls and those in which some degree of atrophy is present in the skin, but also those in which this feature is completely absent; in other words this process (*Dermatophorie*) can detect early changes in the hands of radiologists which a naked-eye inspection cannot do. *S. Russ*

BALLESIO, P. L. & CLAVENZANI, E. Studio sulla intensità delle radiazioni diffuse nella diagnostica radiologica. Nota I. Sezione per l'apparato digerente. [**The Intensity of Radiation in Diagnostic Radiology. I. Digestive Apparatus**] *Rass. Med. Indust.* Rome. 1958, Nov.–Dec., v. 27, No. 6, 598–614, 7 figs. [19 refs.] English summary (9 lines).

TULLIS, J. L. **Delayed Effects of Ionizing Radiations in Man.** *Arch. Pathology.* 1958, Oct., v. 66, No. 4, 403–17. [128 refs.]

The author, in a very valuable paper, cites as an extreme case of delayed action "a woman who at the age of 21 was subjected to a diagnostic roentgen examination lasting for about one hour for kidney stones. It was estimated that the skin dose was about 2000 r of 100 kv. An acute dermatitis resulted after two weeks, but this healed. Later the skin became atrophic, but it was not until 49 years after the original examination that ulceration in the irradiated area occurred which on biopsy was found to be squamous-cell carcinoma."

The author passes in review the tissues or systems which have given evidence of latency leading to some definite pathological effect. These are discussed under the headings of the skin, leukaemia, thyroid cancer, congenital hazards, the respiratory system, lesions in dial painters and in patients treated with radium salts, lesions in patients with retained colloidal thorium dioxide (Thorotrast), bone, nasopharynx, female pelvic organs, late haematological effects, cataracts, shortening of life span and aging.

The data are drawn almost exclusively from cases arising out of the medical use of ionizing radiations and the author has put readers in his debt by a list of 128 references arranged in alphabetical order. The paper should serve as a most useful reference paper.

S. Russ

HARTWIG, Q. L., LEFFINGWELL, T. P. & MELVILLE, G. S. **Some Toxic Effects of Yttrium and Lanthanum. Toxicological Studies with Yttrium and Lanthanum Nitrate as modified by Site of Injection and Whole-Body Radiation.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 505–10, 4 figs.

Though this study was designed to investigate the toxicity of the stable isotopes of the fission products yttrium and lanthanum, their administration to rats indicated some effects which would be possible after nuclear reactor accidents and also in cancer therapy if such rare earths are given along with the radio-active element in order to limit diffusion in the body. Cumulative lethal effects were noted when yttrium nitrate was present in substantial amounts, 350 mgm./kgm. intraperitoneally, and when the rat also received acute exposure to 800 r of ^{60}Co gamma rays. These yttrium plus radiation animals had a higher mortality than those receiving either alone, and deaths in rats receiving yttrium plus radiation were twice as many as in rats receiving yttrium alone. Mortality in a smaller group given 450 mgm./kgm. lanthanum nitrate plus radiation followed a similar acute toxicity trend, with the deaths slightly delayed. Subcutaneous injection of 200 mgm. yttrium or lanthanum nitrate in 1 ml. water caused abscess formation, sloughing and epilation, whereas with sodium nitrate or saline solutions no such effects occurred. The large abscesses remained localized and were apparently painless and non-infected. Impregnation of incisions on the backs of rats, previously irradiated, with 140 mgm. yttrium nitrate or 180 mgm. lanthanum nitrate, as powder, caused abscesses and delay in healing, but not with 180 mgm. sodium nitrate. Healing, complete in 15 days in the last mentioned group, was in the other 2 retarded for weeks. The implication of these results to man is in the effect of rare earths which may be introduced into lacerations from a reactor explosion. *M. Patricia Fitzsimons*

Atmospheric Pollution

WELFORD, G. A., SUTTON, Doris C., MORSE, R. S. & TARRAS, S. **Determination of Thorium in Urine.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 464–8, 1 fig. [11 refs.]

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 157. **Air Pollution. Fifth Report of the Expert Committee on Environmental Sanitation, Geneva, 18–23 November 1957.** 26 pp. 1958. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

This valuable report consists of a survey of all aspects of air pollution with suggestions for future research and for preventive action. It is primarily intended for doctors, engineers and administrators who are facing air pollution problems for the first time.

After a brief introduction, the nature of pollution and the factors favouring its accumulation are described, and methods of measurement are outlined. The effects it produces and its prevention and control are discussed, with special stress on legislative and administrative aspects.

The Committee recommends: (1) standardization of terminology and units of measurement, of the instruments used for measurement and clarification of medical terms used to describe diseases believed to be caused or aggravated by air pollution; (2) research on practically all aspects of the problem; (3) collection and dissemination of scientific, technical and economic information; (4) (a) preparation of pilot schemes of control, (b) organization of national committees to advise on legislation, (c) the use of educative rather than penal methods by enforcement officers, and (d) the establishment of national air pollution advisory councils; (5) the training of staff; (6) the education of the public; (7) publication by WHO of a monograph on air pollution.

J. McK. Ellison

HEMEON, W. C. L., HAINES, G. F. Jr. & IDE, H. M. **Determination of Haze and Smoke Concentrations by Filter Paper Samplers.** *Air Repair.* 1953, v. 3, pp. 22, 11 figs.

This paper describes a method of measuring non-gaseous air pollution. Air is drawn through a filter paper and an index of pollution is obtained from the reduction of optical transmission through the stain left on the paper; this index is expressed in coh units. The method appears to be primarily intended for measuring pollution in factory chimneys, but may also be used for general pollution. The authors stress that a method of this type is preferable to one giving pollution in terms of weight, since the latter gives results which can be dominated by relatively few large particles; the "coh unit", depending on the area of cross-section rather than on the mass of the particles, is more closely related to ability to soil surfaces.

If the light passing through clean filter paper is measured by photometer and gives a reading I_0, and that passing through soiled filter paper is I, then a coh unit is defined as $100 \times \log I_0/I$. It is shown that this unit is additive, *i.e.*, if the pollution deposited on the paper is doubled so also is the reading in coh units [this conclusion is in conflict with the findings of DAWES, J. G., this *Bulletin*, 1955, v. 30, 875, but the discrepancy is small unless the deposit is very heavy]. Hence the stain in these units is proportional to the length of the column of air, of the same area as the filter, drawn through it, and if its coh value is divided by this length the concentration of pollution may be expressed in coh units per thousand feet.

As a crude index of air pollution the method is simple and sensible. The authors do not, however, discuss the effect of colour on the readings obtained; black and white pollutants do not seem likely to be equally effective in obscuring.

J. McK. Ellison

CHOLAK, J., SCHAFER, L. J., YOUNKER, W. J. & YEAGER, D. W. **The Relationship between Sulfur Dioxide and Particulate Matter in the Atmosphere.** *Amer. Indust. Hyg. Ass. J.* 1958, Oct., v. 19, No. 5, 371–7, 8 figs.

This paper describes an "aerometric survey" of atmospheric pollutants in Cincinatti in 1957, and compares this with earlier periods. 2 sites are compared, one in the middle of the commercial centre and one in a residential area in the centre of metropolitan Cincinnati. At each, nitrogen dioxide and oxidants were recorded continuously, sulphur dioxide was sampled sequentially every 2 hours, particulate matter was filtered out of about 2,000 m^3 of air every 24 hours and smoke was filtered on to paper tape during successive 2-hour periods. The results for the two sites are compared on an hour-by-hour basis (1) in the heating season, and (2) outside the heating season. Monthly means are also compared. For the residential site particulate matter and "light scattering potential" were closely correlated (correlation coefficient = 0·82). [No corresponding data seem to have been obtained for the commercial site.] The authors conclude that in coal-burning communities "particulate matter" may be calculated from the light-scattering "coh unit" [see HEMEON *et al.*, above].

J. McK. Ellison

WASSER, R. W. **Sampling Effluent Gases for Particulate Matter.** *Amer. Indust. Hyg. Ass. J.* 1958, Dec., v. 19, No. 6, 469–76, 7 figs.

SHEPHARD, R. J. **Topographic and Meteorological Factors influencing Air Pollution in Cincinnati.** *Arch. Indust. Health.* Chicago. 1959, Jan., v. 19, No. 1, 44–54, 11 figs.

Sanitation

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

BRAZIS, A. R., LESLIE, J. E., KABLER, P. W. & WOODWARD, R. L. **The Inactivation of Spores of *Bacillus globigii* and *Bacillus anthracis* by Free Available Chlorine.** *Applied Microbiol.* Baltimore. 1958, Sept., v. 6, No. 5, 338–42, 7 figs.

This work, conducted at a Sanitary Engineering Center of the United States Public Health Service, was designed to afford "practical information on water treatment plant operation in times of disaster". It affords detailed information about the concentrations of available chlorine required to kill spores of *Bacillus anthracis* and *B. globigii* in water in different periods of time, at different temperatures and at different *p*H levels from 6·2 to 10·5. *B. globigii* was found to be more resistant than *B. anthracis* except at *p*H 9·5 or more (when in any case the effective concentration of chlorine is impracticably high): it is therefore considered a satisfactory "index organism". *L. P. Garrod*

VELICANGIL, S. & DEMIRHINDI, O. Zur Frage eines kombinierten Verfahrens der Kohlehydratspaltung und Indolbildung bei der Diagnose der Coliformen Bakterien. [**A Combined Method for the Isolation and Identification of Coliform Bacteria**] *Arch. f. Hyg. u. Bakt.* 1958, Dec., v. 142, No. 8, 588–93. [15 refs.]

The authors, from Istanbul, have combined in a single tube the media for demonstrating fermentation of carbohydrate and indole production. They have also adapted it to a temperature of 44°C. It is particularly useful for the identification of coliform organisms of faecal origin. [The references at the end of this paper are silent as to recent British work on the rapid identification of *Escherichia coli*.] *E. Windle Taylor*

ZIMMERMANN, W. Zur Hygiene der Mineralwasserfabrikation. I. Ergebnisse von Besichtigungen und Untersuchungen. [**The Hygiene of Mineral Water Manufacture. I. Results of Survey and Investigations**] *Arch. f. Hyg. u. Bakt.* 1958, Dec., v. 142, No. 8, 609–25, 9 figs. [11 refs.]

The great popularity of bottled natural mineral waters in West Germany where these drinks are believed to promote good health led to the investigations which are described in this paper. A table derived from a publication of 1954 sets out that West Germany produced 667 million litres of bottled mineral water and lemonade or 13·3 litres per head per annum, England's consumption was 12·7 litres, France's was 18·6 litres and Sweden's 25·0 litres per head per annum.

In West Germany there are 4,800 small and large factories which produce these bottled drinks. The natural mineral waters are treated to remove iron when necessary and then carbonated before bottling. The investigations which are described at some length consisted mainly of bacteriological analysis of samples of water taken from the original wells, at different stages in the bottling factory and from bottles with different types of stoppers. There is an account with photographs of methods in use for bottling in which attention is drawn to the chances of pollution of the mineral water by the hands of the bottlers. As a rule oligodynamic silver preparations are added to sweet drinks such as lemonade and this treatment is shown to be effective in killing bacteria which may have been present in the liquid beforehand.

The main conclusion is that when bacterial contamination of the processed drink is found it is due mainly to the processing where the water is kept in tanks and some of the bottles are not sterile. Most important of all is the stage of bottling in which the hands of workers may contaminate the contents of the bottles particularly when these are closed by screw stoppers.

M. E. Delafield

RHEINFURTH, H. Zur Hygiene der Mineralwasserfabrikation. II. Gesundheitspolizeiliche Folgerungen. [**The Hygiene of Mineral Water Manufacture. II. Public Health Aspects**] *Arch. f. Hyg. u. Bakt.* 1958, Dec., v. 142, No. 8, 626–31.

In this paper there is a description and discussion of the legal powers of the public health authority to maintain or secure good hygienic practice in the mineral water bottling industry. Under existing legal enactment the medical officer of health has certain powers such as of entry to factories for inspection and the taking of samples but there should also be full practical cooperation between the public health authority and such organizations as the Institute of Hygiene and the Medical Examination Office.

There is particular reference to the existing hygienic defects described in the previous paper (*vide supra*) with a list of recommendations for securing the removal of these defects. These measures include the regular bacteriological control of the well from which the mineral water is derived and of the water during and after processing, adequate cleaning and sterilization of bottles, machine filling and stoppering of bottles and annual examination of personnel for skin disease, suppurating wounds and the bacterial carrier state.

M. E. Delafield

JACKSON, D. & WEIDMANN, S. M. **Fluorine in Human Bone related to Age and the Water Supply of Different Regions.** *J. Path. & Bact.* 1958, Oct., v. 76, No. 2, 451–9, 1 fig. [19 refs.]

The authors ascertained the fluorine content of normal human bone (6th rib) in order to discover how far it may be influenced by variations in the dose of fluorine and time of exposure. They chose 3 regions of England with substantial differences in the fluorine content of the drinking water:

(a) Leeds—water supply containing virtually no fluorine (42 specimens)

(b) South Shields—water supply containing at present 0·8 p.p.m. (27 specimens)
(c) West Hartlepool—water supply containing 1·9 p.p.m. (56 specimens).

The South Shields figure is lower than that of 10 years ago because of recent additions of moorland water supplies.

In Leeds there was a steady increase in the fluorine uptake from the age of 12 to 40 years, after which the rate of increase lessened until a plateau was reached at the age of 55. This equilibrium is reached when the fluorine content approximates to 190 mgm. F. per 100 gm. bone.

In South Shields there was an identical pattern of fluorine uptake, the plateau being reached at age 50–60, with a fluorine content only 25% greater than the Leeds plateau figure.

In West Hartlepool, the plateau was reached at about 55 years of age, but the fluorine content approximated to 400 mgm. per 100 gm. bone—a level twice as high as that found in Leeds.

It might be expected that since the Leeds water contains practically no fluorine there would be no appreciable increase of bone fluorine in Leeds as age advances, but the authors' findings show that even in the absence of water-borne fluorine there is at least a 10-fold increase in bone fluorine in Leeds between the ages of 13 and 50 years. It is possible that there is some other source of fluorine, and the authors suggest that this is probably tea leaves. *Robert Weaver*

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

Reploh, H. & Gängel, G. Hygienische und bodenmikrobiologische Untersuchungen auf den Landbehandlungsflächen der Stadt Bielefeld. [**Hygienic and Microbiological Studies of Irrigated Sewage Fields in Bielefeld, Germany**] *Arch. f. Hyg. u. Bakt.* 1958, Dec., v. 142, No. 8, 594–608, 1 map. [13 refs.]

The character of the systems of water supply and sewage disposal in the city of Bielefeld made it possible to carry out microbiological, hygienic and chemical investigations in connexion with the sewage irrigation of fields which had not previously been treated in this way. In this paper there is a description of the geography of the water collection system with a map. The methods employed for the examination of water, soil and plant samples are stated and the results of various investigations are described at considerable length with tables of numerical data.

Salmonellae were isolated from the irrigated land on only a few occasions although the crude sewage and partially treated sewage were found frequently to contain these organisms. Some experiments on the survival of typhoid and paratyphoid organisms inoculated into the sandy soil showed that these bacteria could be isolated even after 24 weeks from the sterilized soil but not after about 8 weeks from unsterilized soil. Investigations were also made of the *Escherichia coli* titre and total bacterial count of the soil on the surface and at various depths after the fields had been irrigated. Some study of the fungal forms at different depths in the soil was made. No helminth eggs were found. Chemical analyses of the chloride, sulphate, nitrate, nitrite, ammonia and free carbon dioxide content of water from sampling wells at the border and at 300 metres distance from the irrigation area were carried out.

M. E. Delafield

Bloom, H. H., Mack, W. N. & Mallmann, W. L. **Enteric Viruses and Salmonellae Isolation. II. Media Comparison for Salmonellae.** *Sewage & Indust. Wastes.* Wash. 1958, Dec., v. 30, No. 12, 1455–60. [11 refs.]

Selenite brilliant green enrichment medium was found superior to tetrathionate broth for the isolation of *Salmonella* from sewage. The medium is described by J. L. Stokes and W. W. Osborne [*Applied Microbiol.*, 1955, v. 3, No. 4, 217; this *Bulletin*, 1956, v. 31, (444)].

[For Part I of this study, see this *Bulletin*, 1959, v. 34, 259.] *E. Windle Taylor*

Peel, C. **The Public Health and Economic Aspects of Composting in Tropical Africa.** *Sanitarian.* London. 1959, Jan., v. 67, No. 4, 238–45, 1 fig. [18 refs.]

In view of low nutritional levels and population expansion in British African territories the author of this paper contends that agricultural development and public health activities must go hand in hand. Mixed farming would enrich the soil but many tribes are not cattle-owning and the tsetse also sets limits. Chemical fertilizers are too expensive for general use in Africa but human and other organic wastes when composted yield nutrients that maintain and improve soil fertility. The selection of a particular system of composting depends on local conditions and a pilot project should be tried. Composting by the Indore process was introduced into Northern Nigeria in 1941 and now many towns and villages have composting installations. In Kano with a population of 130,000 5 large installations are working continuously dealing with 3,000 bucket latrines and city garbage and litter, together with the paunch contents from 2 abattoirs. Many thousands of tons of compost are applied annually to the soil and composting has become an important and integral part of the agricultural economy. There has proved to be no public health hazard if the operation is properly supervised. The system of composting used is described and a plan of the layout is shown. Short appendices give actual temperatures of composting operations in Kano, reaching nearly 70°C., and demographic data from British African territories showing the rates of increase.

This is an excellent account of the case for composting and a general description of the Indore process.

T. H. Davey

MARWAH, S. N. **An Experiment in Interruption of Man-to-Man Faecal and Helminthic Circulation in Rural Community.** *J. Indian Med. Ass.* 1958, Nov. 16, v. 31, No. 10, 403–8, 2 figs.

This paper lists very briefly the various types of simple rural latrines and describes objections to them. In a sanitation campaign in India the type mainly constructed was the "Lal" type [see this *Bulletin*, 1951, v. 26, 525] in which a slightly tapering straight pipe leads without any water seal from the pan in the squatting plate into a trench. Objections to this were that the cover over the trench collapsed, that particles of faecal matter stuck to the unglazed pipe and that the 6-inch aperture of the pipe was too small for the direct reception of faeces, so that soiling of the pan occurred. 2 improved types of latrine based on this model were introduced. In one the pan and pipe were cast in one piece in a clay mould and were "glazed" by rubbing with white cement before curing. The pipe discharged into the middle of a trench 10′ × 2′ × 3′ or a pit 10′ × 2½′. The second type was devised to meet the problem of covering the trench or pit. The pan with an attached pipe was incorporated in and projected a little beyond the front edge of a squatting slab 3′ square. The slab and latrine were set on a brick base over a pit 10′ × 2½′. In this design no further covering over the pit is necessary, faecal matter is invisible, no extra water is needed for flushing and though there is no water seal there is no nuisance.

T. H. Davey

ERRATUM

The paper by CHRISTOVÁO on the significance of the coliform index [this *Bulletin*, 1958, v. 33, 967] contains an incorrect formula. The figure 0·465 should be represented as a power of the expression in parentheses and not as a factor.

The correct formula is:

$$I_{cc}=I_{sc}\left(\frac{R_{sm}}{R_{om}}\right)^{0\cdot465}$$

Food and Nutrition

FOODSTUFFS

Composition and Bacteriological Control

DI SAPIO, G. Ricerche sotto il profilo igienico su 104 campioni di burro del mercato della città di Napoli. [**The Condition of 104 Samples of Butter Marketed in Naples**] *Igiene e San. Pubblica.* Rome. 1958, Sept.–Oct., v. 14, Nos. 9/10, 496–505. English summary (7 lines).

This report deals with the result of bacteriological examination of 20 samples of butter from 2 large butter factories from the north of Italy, and 84 from small plants in or near the city. 8 of the factory samples were labelled pasteurized and 12 non-pasteurized, while all the local samples were non-pasteurized. They were all bought in Naples and its environs between October 1957 and April 1958 and all were wrapped in tinfoil or grease proof paper.

After suitable dilutions had been made examinations for total bacteria, *Escherichia coli* and yeast counts were carried out on all samples; 60 were examined for *Mycobacterium tuberculosis*, *Brucella*, and other pathogens.

The results were that in practically all the tests the local products showed up best, particularly in the *E. coli* count as no less than 40 out of 84 gave less than 10 *E. coli* per cc., and 37 between 10 and 100. Tubercle bacilli of bovine type were found in 1 of 20 industrial samples and 1 of 40 local plants, but no other pathogens were found.

Di Sapio mentions that in general the results of the various tests ran parallel, so taking a total count of 10^5, with *E. coli* absent in 0·1 cc. as practical limits, the factory samples showed quite a high degree of contamination even in 4 samples made from pasteurized cream. He explains this by the length of time taken in transport compared with the local products, but he considers that the examinations have shown that if properly guided and helped, the local plants are capable of supplying a reasonably satisfactory product.

W. K. Dunscombe

CIOGLIA, L. & ARU, L. Sul controllo igienico dei frutti di mare. [**The Hygienic Control of Shellfish, etc.**] *Nuovi Ann. d' Igiene e Microbiol.* 1958, July–August, v. 9, No. 4, 285–323. [29 refs.] English summary.

The problems connected with shellfish control can be those arising from the nature of the breeding ground, those associated with the tests for purity and those linked with marketing. This paper, by workers from the University of Cagliari, Sardinia, is a study of edible shellfish and of sea-urchins to determine their normal bacterial flora and that deriving from pollution; it also served to establish techniques and their simplification and standardization. The shellfish examined were varieties of mussels (*Mytilus galloprovincialis*, *Venus decussata*, *Cardium tuberculatum*) together with sea-urchins (*Paracentrotus lividus*), which are most commonly consumed in Cagliari. In all tests the dry weight of the sample should be considered to make standardization possible. *Mytilus galloprovincialis* is 4·24 times heavier than the black mussel (*Venus decussata*), and 4·46 times than the white mussel (*Cardium tuberculatum*) but is only 0·63 of the weight of the sea-urchin, so

that if 100 *Escherichia coli* organisms are permissible in each *M. galloprovincialis*, then 23 to 24 *E. coli* are allowed in a black mussel, 28 to 29 in a white mussel, and 158 in a sea-urchin.

On the basis of such standards, a considerable proportion of "sea-fruit" on sale in Cagliari is polluted. It is also thought that some molluscs, in spite of being certified as to origin and purity, are still unsatisfactory. Pollution probably occurs when winds produce a current which takes to the mollusc beds effluent from the city.

The presence of enterococci (group D streptococci) proved to be a useful index. A search for salmonellae and shigellae was negative, while some *Proteus* strains were met with. The presence of *Proteus* tends to indicate pollution, but its occurrence in faeces is not constant enough for it to serve as an index. Tests based on the presence of *Clostridium welchii* do not appear practicable. An interesting investigation was made into the presence in molluscs of "terrestrial" and "marine" bacteria, showing a great preponderance of the latter. An increase in the number of "terrestrial" bacteria and of *E. coli*, coliforms and enterococci go together. The number of chromogenic bacteria is inversely related to the degree of pollution. A high count of marine micro-organisms can be found even in molluscs which have been lying in water free from pollution, but rich in plankton. This should not be the case in molluscs which have been undergoing artificial purification. Mussels tend to accumulate bacteria in their digestive apparatus of which a bacterial count is much higher than those of sea water and mud in which they may be lying.

The investigation has shown that bacterial control should be more searching, the *E. coli* test alone being insufficient. The authors advise the use of a coliform count, an enterococcal count and a count for "terrestrial" micro-organisms, after selective heating to 43°C. for 10 minutes and culture in agar and in gelatin. These 3 tests in combination are the most useful.

Several formulae for media used in cultivating marine micro-organisms are given. *E. Agius*

FOOD POISONING

Sapeika, N. **Mussel Poisoning: a Recent Outbreak.** *South African Med. J.* 1958, May 17, v. 32, No. 20, 527.

The author recalls several cases of mussel poisoning (2 of which were fatal) occurring near Durban and, far away, near Cape Town in 1957–8. Black mussels of the variety *Mytilus* were responsible, and the author examined specimens collected in the Cape area. Extracts of cooked and uncooked mussels were highly toxic to rats and cats, and extracts of the digestive apparatus were especially so. The poison is not destroyed by heat, and though its chemical structure is not known, it is regarded as an alkaloid. It is derived from plankton taken in by the mussels, and these may be so abundant as to give a reddish colour to the sea. In the north Pacific the plankton is *Gonyaulax catenella*, but on the west cost of South Africa it is *Gymnodinium*, prevalent in spring and autumn.

The poison has an extremely strong neurotoxic and peripheral neuromuscular action, and depresses the circulatory system; there is no specific antidote, and treatment therefore consists of gastric lavage with sodium bicarbonate, purgation, artificial respiration and the use of pressor drugs.

Clams and oysters may be poisonous from the same cause, and a single specimen may contain a fatal dose.

[See also this *Bulletin*, 1958, v. 33, 155.]

Charles Wilcocks

Vor Dem Esche, P. & Handloser, M. Zur Frage der Verbreitung von Salmonellosen durch Hühnereier. [**The Spread of Salmonella Infections from Hens' Eggs**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 304–19. [Numerous refs.]

The occurrence of 2 epidemics of gastro-enteritis due to *Salmonella typhi-murium* in the town of Brackwede and district in 1956–7 focussed attention on the possibility of hens' eggs having been the origin of the infections. In the first of these epidemics 259 persons were notified from 4 areas around Brackwede and 127 of these were proved by bacteriological investigation to be cases of *Salm. typhi-murium* infection. These cases followed a few days after 16 cases of gastro-enteritis from the town itself had been reported. The factor common to these cases was the consumption of cream cakes and tarts of various kinds all of which were distributed by 1 firm to the city and surroundings. Investigation of these bakery products proved that the causal salmonella could constantly be isolated from the cream. There is a detailed account of the bacteriological study of the constituents of the cakes and the cream which was carried out. It is presumed that hens' eggs may have been the source of the infection since ducks' eggs could be excluded from suspicion. As eggs were not used in the cream itself it is considered to be probable that it became contaminated in the course of mixing in mixers previously used for the dough of the cakes and tarts which contained eggs.

There is a considerable discussion of the question of infection of hens' eggs with some emphasis on the possibility of secondary infection. In some experiments it was shown that a number of different bacteria can penetrate the shell of hen's eggs from outside in a period of 24 to 72 hours of incubation at 37°C. The bacteria were isolated more frequently from the yolk than from the white of the egg which appears to indicate that the white has some inhibitory action on bacterial growth. *M. E. Delafield*

Nikodemusz, I. *Bacillus cereus* als Ursache von Lebensmittelvergiftungen. [*Bacillus cereus* **as a Cause of Food Poisoning**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 335–8. [21 refs.]

Out of 175 persons employed in a business organization near Budapest, 65 were taken ill with profuse

diarrhoea between 4 and 16 hours after their midday meal. Some of the sufferers complained of nausea but none had vomiting, fever or malaise and all had recovered within 24 hours.

From a sample of vegetable soup consumed at the meal a Gram-positive, aerobic spore-bearer was found in large numbers and scarcely any other organisms were isolated. The spore count was 3,600 per gm. The organism was diagnosed as *Bacillus cereus* on its growth and biochemical reactions which are described.

Hitherto no reports of the association of *B. cereus* with food poisoning have been published in Hungary although several accounts of this association have appeared in the literature of other countries [this *Bulletin*, 1956, v. 31, 660; 1958, v. 33, 682].

M. E. Delafield

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 147. **Expert Committee on Biological Standardization. Eleventh Report.** Geneva, 16–21 September 1957. 38 pp. [Refs. in footnotes.] Geneva: 1958. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

Like the Tenth Report [this *Bulletin*, 1957, v. 32, 1085], this relates to antibiotics, hormones, antigens, antibodies, and certain miscellaneous substances, giving a few lines of text commentary for each. There is an annex on International Biological Standards and Reference Preparations, 1958, in which a long table (occupying 8 double pages) is incorporated which gives, for a long series of preparations, information on international units, the form in which the substance is dispensed, dates of establishment of standards, and references to the literature. *Charles Wilcocks*

HACKENTHAL, H. & BIERKOWSKI, E. Studien über bakterielle Mischungen. [**Studies on Bacterial Mixtures**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 5/6, 431–61.

Micro-organisms may be grown on an optimum nutrient medium or on an inferior medium. On an optimum medium the individual colonies resemble one another and the colonies of organisms from which they are derived and subculture gives a similar picture. The biochemical characteristics of the organisms also remain similar. These are the criteria of a pure culture. A pure culture from an optimum medium sometimes shows morphological and even serological changes when grown on an indifferent medium, due to proliferation of organisms which were subdued and overgrown by the main organism in the supposed pure culture on an optimum medium. In any bacteriological investigation therefore it is important to use not only optimum media for the organism cultivated but also indifferent media to detect the presence of other organisms in the supposed pure culture. A "functional" pure culture is defined as a stock culture which has been purified so far from other organisms that it shows constant colony form and chemical characteristics. A perfectly pure culture is almost impossible to obtain even from a single cell culture and the higher the degree of purity the worse the growth. One component of a "functional" pure culture can assume all the reactions—serological and biochemical—of another component as long as it grows in the community. It is suggested that ability to grow in a colony requires a mixture of organisms and that a really pure strain cannot grow in colonies. *P. A. Clearkin*

KANZ, E. Bakterienkultivierung im Symbioseverfahren durch eine neue Form der Ammenplatte. [**Bacterial Culture in Symbiosis by Means of a New Type of Culture Plate**] *Arch. f. Hyg. u. Bakt.* 1958, June & Aug., v. 142, Nos. 4 & 5, 288–320; 321–38, 21 figs. [46 refs.]

Cultures were carried out in a Petri dish with 2 layers of nutrient media separated by a layer of Cellophane. The test organism was grown on the upper layer above the Cellophane and the "foster mother" organisms on the layer below the Cellophane.

Experiments showed that growth of *Clostridium tetani* on the upper layer above the Cellophane was enhanced by *Chromobacterium prodigiosum* or of *Pseudomonas pyocyanea* grown simultaneously below the Cellophane. *Ps. pyocyanea* in addition to a stimulating effect on growth of *Cl. tetani* inhibited the growth of staphylococci, and hence could be used to obtain pure cultures of tetanus bacilli from a mixed infection.

Growth of *Haemophilus influenzae* was stimulated by culture in symbiosis with *Staphylococcus pyogenes aureus* and *Micrococcus catarrhalis*. During the course of the experiments 2 other organisms were found which also stimulated growth. Both were Gram-positive cocci, one was haemolytic and the other non-haemolytic.

Stains can be incorporated in the medium and the organisms thus stained vitally during growth. The Cellophane being transparent the colonies can be studied under the microscope and moreover the membrane can be dried, fixed and filled for future reference complete with the colonies. *P. A. Clearkin*

HIRSCH, A., CATTANEO, C. & MORELLINI, M. Zur Frage der Reduzierung von 2,3,5-Triphenyl-tetrazoliumchloride durch Mikroorganismen verschiedener Familienzugehörigkeit. [**Reduction of 2,3,5-Triphenyl-tetrazolium Chloride by Micro-organisms of Different Families**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 355–66. [Numerous refs.]

The authors have extended their studies on the value of irreversible reduction of 2,3,5-triphenyl-tetrazolium-chloride for differentiating among bacterial strains as previously described [this *Bulletin,* 1959, v. 34, 274].

The outcome of a study of a variety of ways in which the substance may be used has led the authors to the conclusion that the best differentiation can be obtained if 0·05 gm. of the compound is dissolved in 100 ml. of 1/30 M buffer solution and 3 or 4 drops of this reagent are rubbed up with 5 mgm. of bacteria on a white tile, the reading being taken after 1 hour at room temperature. The colour, graded from light rose to deep purple, indicates the strength of the reaction.

Using a series of buffers (*p*H 2·8, 5·0, 7·0, 9·1 and 12·5) and examining 95 strains from 11 different families and 2 yeast forms, they reached the following conclusions:—

No bacterial or yeast forms reduced at the lowest *p*H whereas all reduced at the highest. At *p*H 7·0, however, frank distinctions were obtained; thus active reduction is observed with many *Pseudomonas* forms, with *Serratia,* with *Staphylococcus,* with *Sarcina,* with the bacillaceae, and mycobacteriaceae and with one of the species of *Candida* investigated, but not with *Escherichia, Proteus, Salmonella, Shigella, Brucella, Streptococcus. Clostridium* or *Nocardia.* It is obvious from the above list that there is a general tendency for the reduction of tetrazolium at *p*H levels in the vicinity of neutrality to go with Gram-positive staining.

There is a tendency in the groups in which reduction does occur at this *p*H level for it to be most pronounced with the non-pathogenic forms and the difference in degree of reduction is held to be a valid ground of distinction between pathogenic and non-pathogenic forms among the mycobacteria and the candidae.

J. W. McLeod

CATLIN, B. W. & CUNNINGHAM, L. S. **Studies of Extracellular and Intracellular Bacterial Deoxyribonucleic Acids.** *J. General Microbiol.* 1958, Dec., v. 19, No. 3, 522–39, 1 fig. [Numerous refs.]

"Highly polymerized bacterial deoxyribonucleic acids (DNAs) obtained from extracellular and from intracellular locations were analysed. DNAs from two strains (*Staphylococcus aureus* and *S. epidermidis*) were of the type having high adenine and thymine contents; two others (*Alcaligenes faecalis* and *Pseudomonas fluorescens*) had a high content of guanine and cytosine. For each micro-organism the composition of extracellular DNA was essentially the same as that of the intracellular DNA. Conditions associated with the extracellular accumulation of DNA in cultures of 3 strains were investigated. *S. aureus* elaborated a deoxyribonuclease (DNase) which required calcium ion and high pH for activity. In a culture medium of *c.* pH 6 and insufficient calcium, the DNase was inactive and DNA slime accumulated. In cultures of *P. fluorescens* a specific ribonuclease-sensitive DNase inhibitor protected slime DNA from depolymerization by culture DNase. In cultures of *A. faecalis,* also, both a DNA slime and a low concentration of DNase may occur. This enzyme, detected by studying its action against solutions of calf thymus DNA prepared from dried fibres, was activated by various cations within the pH range of cultures. Unlike other DNases, however, it has little capacity to attack the slimelayer DNA, which presumably is more nearly native."

MCCARTHY, B. J. & HINSHELWOOD, C. **Variations in Catalase Activity during a Bacterial Growth Cycle.** *Proc. Roy. Soc.* Ser. B. 1959, Jan. 27, v. 150, No. 938, 13–23, 9 figs.

OLITZKI, A. L. **The Infection Promoting Substances (a Review).** *Bull. Res. Counc. of Israel.* 1957, Dec., v. 6E, Nos. 3/4, 193–222, 1 fig. [237 refs.]

In this review only infection-promoting substances which act under experimental conditions are discussed. The author gives a very full account of the substances, particularly mucin which have been used to help establish peritoneal infections. This is followed by 2 short sections on the lowering of host resistance by alterations in metabolic processes and by cortisone and ACTH. The effect which antibiotics have on the development of secondary infection by disturbing the normal bacterial flora is also mentioned. Then the production of enteric infections by neutralizing the acidity of the stomach and increasing the permeability of the intestinal wall is discussed in detail. Methods of establishing lobar pneumonia with materials which occlude the air passages and with irritants such as lewisite, phosgene or ether are described. Details are given of substances, including Ca ions, which help to produce local infections by toxigenic bacteria. The review ends with a brief description of the enhancement of local infections by spreading factors. *Sheila McDonald*

i. KIES, Marian W., ALVORD, E. C., Jr. & ROBOZ, Elizabeth. **Production of Experimental Allergic Encephalomyelitis in Guinea Pigs with Fractions isolated from Bovine Spinal Cord and Killed Tubercle Bacilli.** *Nature.* 1958, July 12, v. 182, 104–5.

ii. COLOVER, J. **Experimental Allergic Encephalomyelitis induced with Combined "Purified" Spinal Cord and Bacillary Fractions.** *Ibid.,* 105–6.

i. These two papers record experiments on the production of experimental allergic encephalomyelitis in

guineapigs with fractions prepared from tubercle bacilli and bovine spinal cord. Details should be sought in the originals, but Kies *et al.* state that their experiments are preliminary in the sense that the fractions tested are mostly not pure compounds.

ii. Colover remarks that the experiments show that allergic encephalomyelitis can be produced in guineapigs by emulsions containing only relatively small fractions of acid-fast bacilli and central nervous tissue, and that either of 2 constituents of tubercle bacilli (residue 1/172 and wax *D* Canetti) mixed with either of 2 bovine spinal cord protein fractions can be effective. *Charles Wilcocks*

SCOTT, W. J. **The Effects of Residual Water on the Survival of Dried Bacteria during Storage.** *J. General Microbiol.* 1958, Dec., v. 19, No. 3, 624–33, 6 figs. [13 refs.]

After primary drying of bacteria the unsealed ampoules were placed inside larger tubes (which were sealed later) containing substances of known water activity. After storage at 25°C. ampoules were opened at intervals and viable counts were made on the dried material.

When the test organisms (*Staphylococcus aureus*, *Pseudomonas fluorescens*) were dried in casein digest medium the best survival was obtained with a trace of residual moisture. Salmonella Newport survived well in casein digest when the moisture content was low and the ampoules were sealed *in vacuo*, but when sealed in air the relations between survival and water content were reversed within the limits tested.

The addition of glucose or sucrose to the suspending fluid was beneficial, and the drier the end product, the better the survival of the test organism. Those interested in the preservation of bacteria by freeze-drying should read this paper for details. *S. T. Cowan*

BROWN, C. E. & GRIFFITH, W. R. **Syringe Device for Studies on Bacterial and other Aerosols.** *Arch. Indust. Health.* Chicago. 1958, Nov., v. 18, No. 5, 415–21, 2 figs. [16 refs.]

This paper describes an apparatus for generating an aerosol and observing its decay; it was designed to be workable by a single individual and capable of performing tests on 50 aerosols in an 8-hour day. The aerosol is generated by a syringe-operated Vaponefrin spray in a 100 ml. jar. After 30 seconds a sample of 1 to 10 ml. of the aerosol is withdrawn by means of another syringe and transferred to the aerosol holding chamber. which is a 100 ml. syringe, in which it can be diluted as required. From this last syringe the aerosol is slowly ejected mechanically and collected in a slit sampler. [Possible fallacies arising from loss of the airborne particles in the narrow tubes and small volumes are not discussed.] *R. E. O. Williams*

ANDERSEN, A. A. **New Sampler for the Collection, Sizing and Enumeration of Viable Airborne Particles.** *J. Bacteriology.* 1958, Nov., v. 76, No. 5, 471–84, 7 figs. [15 refs.]

This paper describes a 6-stage sieve sampler designed to distribute airborne bacteria-carrying particles into 6 size ranges each on a separate culture plate. The 6 stages all have 400 holes in the sieve plate, but the holes are successively of smaller diameter so that smaller and smaller particles are impinged as the air proceeds through the instrument. The first stage collects particles down to about 8 μ in diameter, the last collects particles below 1 μ. The sampling rate is 1 cu.ft. per minute.

As with all sieve samplers there is a risk of overlap of colonies arising from particles traversing 1 hole in the slit. For this reason the author recommends counting the number of holes yielding a colony and provides a table for estimating from the "corrected particle count". [Counts of specific organisms in a mixed cloud could not, however, be obtained by this method.]

No particles from a *Serratia marcescens* [*Chromobacterium prodigiosum*] aerosol were found on membrane filters exposed in the effluent from the sampler. No spores could be recovered by swabbing the interior of the sampler after exposure in a heavy cloud of *Bacillus subtilis*. *R. E. O. Williams*

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order: General; Antibiotics; Other Therapeutic Substances; Disinfection.

WILLIAMS, S. W., MATHEWS, A. G. & HARCOURT, H. K. **The Absorption of Penicillin V in Children.** *Med. J. Australia.* 1958, July 26, v. 2, No. 4, 117–20, 4 figs. [10 refs.]

There being little information about the absorption of newer forms of oral penicillin in children, these authors gave single doses of 4 different forms to 9 children aged from 5 to 13 years, and determined the penicillin content of the blood after 4 and 6 hours and the output in the urine up to 10 hours. The experiment was complicated by variations in the body weight of the subjects (16–42 kgm.) given a constant dose of 200,000 units, and by dividing them into groups of 3 receiving the dose before, during and after breakfast. There was also a rather wide scatter in the results of both blood and urine estimations which makes it seem doubtful whether any but the following conclusion is justified, namely, that all 3 forms of penicillin V, the free acid, calcium salt and potassium salt, produced higher blood levels, usually adequate for therapeutic effect up to 4 hours, than penicillin G (potassium salt): the urinary excretions of penicillin V were also in general higher. *L. P. Garrod*

WHEATLEY, D. **Oral Penicillin in General Practice.** *Brit. Med. J.* 1958, Oct. 11, 907–9.

The Northern Home Counties Faculty of the College of General Practitioners asked its 180 members to reply

to a questionnaire about their use of oral penicillin and 85 did so. The replies are analysed in detail and provide interesting information. Only 5 doctors did not use oral penicillin, and of the remaining 80, 66 gave it to both children and adults and 14 to children only. In a 20-day period over which it was asked that records should be kept, 1,043 doses (73%) were given orally and 379 (27%) by injection, the total number of doses given by an individual doctor in this time varying from 1 to 104. 75% regarded the oral and parenteral route as equally efficacious: of the 25% who regarded the oral as inferior some were probably giving inadequate doses. Penicillin V was used by the majority (75% in adults and 65% in children): other preparations in the order of frequency of their use were benzathine penicillin, penicillin G, and penicillin-sulphonamide mixtures. The main indications mentioned in order of their frequency were tonsillitis, acute otitis media, acute bronchitis, pneumonia, furunculosis and finger infections. Information is also given about the dosage used.

L. P. Garrod

FRASER, H. **Immediate Anaphylactic Shock from Oral Penicillin.** *Med. J. Australia.* 1958, Dec. 13, v. 2, No. 24, 801.

"A report of a case of an anaphylactic shock occurring a few minutes after the ingestion of oral penicillin is presented. There was deep coma and peripheral circulatory collapse. The condition responded satisfactorily to adrenaline and antihistamine injected intramuscularly."

BALLIO, A., CHAIN, E. B., DENTICE DI ACADIA, F., ROLINSON, G. N. & BATCHELOR, F. R. **Penicillin Derivatives of p-Aminobenzylpenicillin.** [Correspondence.] *Nature.* 1959, Jan. 17, v. 183, 180–81, 1 fig.

THIND, K. S. **A Growth Factor in Extract of *Escherichia coli* replacing Streptomycin in Streptomycin dependent *E. coli*.** *Indian J. Med. Res.* 1958, Sept., v. 46, No. 5, 627–37, 1 graph. [11 refs.]

This author, who writes from Philadelphia, U.S.A., has found that an extract of a streptomycin-sensitive strain of *Escherichia coli* prepared by sonic disruption enables a streptomycin-dependent strain of the same species to grow from a smaller inoculum in a medium not containing streptomycin. There is no mention of any attempt to propagate the organism further in the medium with this addition. [In a discussion of the nature of streptomycin dependence an obviously wrong reference is given in 2 places to a paper which appeared 3 years before streptomycin was discovered.]

L. P. Garrod

SAZ, A. K. & MARTINEZ, L. Marina. **Enzymatic Basis of Resistance to Aureomycin. II. Inhibition of Electron Transport in *Escherichia coli* by Aureomycin.** *J. Biol. Chem.* 1958, Oct., v. 233, No. 4, 1020–22.

Saz and his colleagues have previously reported [this *Bulletin*, 1957, v. 32, 605] that the action of an enzyme extracted from chlortetracycline-sensitive *E. coli* is inhibited by this antibiotic, whereas the enzyme obtained from a resistant variant is correspondingly unaffected. The work reported here is an extension of these observations. Purified extracts of sonically disrupted cells had a high flavin content: the reduction by these extracts of 2,6-dichlorophenol-indophenol was inhibited by low concentrations of chlortetracycline when the extract was made from an antibiotic-sensitive culture, and only by high concentrations when the source was a resistant culture. On the other hand the reduction of ferricyanide by extracts of both sensitive and resistant cultures was inhibited by the antibiotic to about the same extent. It is suggested on the basis of these findings that chlortetracycline may exert its effect by interference with some forms of electron transport. 2 further observations are more difficult to interpret. Fractionation of the phenol-indophenol reductase from sensitive cells sometimes yielded 2 components, one sensitive and one resistant to the antibiotic. Still more disturbing is the fact, briefly mentioned, that experiments with tetracycline or oxytetracycline gave quite different results: *e.g.* there was no difference in the degree of inhibition by these antibiotics of phenol-indophenol reduction by extracts of chlortetracycline-sensitive and -resistant organisms.

L. P. Garrod

TEIXEIRA, Gertrude C. & SCOTT, R. B. **Further Clinical and Laboratory Studies with Novobiocin. I. Treatment of Staphylococcal Infections in Infancy and Childhood. II. Novobiocin Concentrations in the Blood of Newborn Infants and in the Breast Milk of Lactating Mothers.** *Antibiotic Med.* New York. 1958, Oct., v. 5, No. 10, 577–85, 2, figs.

Novobiocin was given orally in a dose of 20–60 mgm./kgm. per day to 14 infants with acute staphylococcal infections, 7 having infections of the air passages and 7 various suppurative lesions elsewhere. The response to treatment was good except in 3, 2 of whom had to be given another antibiotic. A few assays of the drug in the blood were made, the amounts found varying from 15 to 81 μgm./ml., partly depending on the time interval since the last dose. The milk of 3 lactating women who had been given novobiocin was also examined: concentrations of about 3–5 μgm./ml. were found in the milk of 2 of them, whereas in the third it is recorded only as having been <4 μgm./ml.

L. P. Garrod

SACKS, L. E. & PENCE, J. W. **The Influence of pH on the Antibacterial Action of Subtilin A.** *J. General Microbiol.* 1958, Dec., v. 19, No. 3, 542–50, 4 text figs. & 1 fig. on pl. [Numerous refs.]

These workers in a Research Laboratory of the United States Department of Agriculture thought it advisable to study the effect of *p*H on the activity of subtilin A because this antibiotic has been proposed as a preservative for both neutral and acid foods. They studied this by enumerating survivors in media of different *p*H containing a constant amount of subtilin,

by measurements of respiration under similar conditions. and by streaking gradient plates on which separated strips of medium containing different concentrations of subtilin were added at right angles to the *p*H gradient. Square plastic dishes were used for this, and some rather untidy but significant cultures in them are illustrated. The main experiments were done with *Staphylococcus aureus* and *Escherichia coli*: the former was more susceptible as the medium was made more alkaline and the latter as it became more acid. Several other species were tested: one behaved like *Staph. aureus* and 3 like *E. coli* [since these 3 were all Gram-positive, the Gram reaction is evidently not a determinant in this connexion]. It is pointed out that differences in susceptibility with varying *p*H have been found for quaternary ammonium compounds, and it is suggested therefore that these and the surface-active polypeptide antibiotics may act in a similar way.

L. P. Garrod

KAPLAN, M. A., HEINEMANN, B., MYDLINSKI, Irene, BUCKWALTER, F. H., LEIN, J. & HOOPER, I. R. **An Antifungal antibiotic (AYF) produced by a Strain of** *Streptomyces aureofaciens*. *Antibiotics & Chemotherapy*. New York. 1958, Oct., v. 8, No. 10, 491–5, 1 fig. [11 refs.]

This report from Bristol Laboratories Inc., Syracuse, N.Y., records that a strain of *Streptomyces aureofaciens* produces 2 closely related heptaene antibiotics: they are found "primarily" in the mycelium and are extracted from it. The method of extraction and some chemical and physical properties of the antibiotics are described: some of these properties distinguish these antibiotics from amphotericin B, trichomycin, candicidin and ascosin. Minimum inhibitory concentrations for various pathogenic fungi vary from 0·3 to 50 μgm./ml. The LD50 (intraperitoneal) for mice is 3·83 mgm./kgm. and the CD50 by the same route for *Candida albicans* infection is 0·038 mgm./kgm. *L. P. Garrod*

KUTSCHER, A. H., SEGUIN, Lucille, RANKOW, R. M. & PIRO, J. D., with the assistance of J. B. CAMPBELL. **Thiostrepton, a New Antibiotic. Disc Sensitivity Studies.** *Antibiotics & Chemotherapy*. New York. 1958, Nov., v. 8, No. 11, 576–83.

Thiostrepton is a new antibiotic for further information about which the reader is referred to 3 papers in *Antibiotics Annual* 1955–6. This paper mentions one property which sounds unpromising, namely, that it is "insoluble" in water. The authors tested the sensitivity to Thiostrepton, 10 other antibiotics, nitrofurantoin and nitrofurazone of 289 allegedly pathogenic organisms from clinical material: the organisms are divided into 11 categories, some of which are pathogenic species, while others are either not species ("nonhemolytic streptococci", "atypical gram-negative rod") or not usually regarded as pathogenic (*Staphylococcus albus*). The disk method was used, the Thiostrepton disk containing 30 μgm., the others the usual amounts in commercial preparations (not stated here). Organisms are classified as highly, moderately or slightly sensitive and resistant. The whole of the results on this basis are given in small print in a full-page Table, and 2 further pages of Tables provide data about correlation between sensitivity to Thiostrepton and to other antibiotics. Thiostrepton is active against streptococci and staphylococci, and almost without exception inactive, so far as these tests reveal, against all Gram-negative bacilli. Apparently it has not yet been used clinically, and "owing primarily to its high insolubility", is likely to be recommended only for local application. *L. P. Garrod*

BEN-GURION, Renana & HERTMAN, I. **Bacteriocin-like Material produced by** *Pasteurella pestis*. *J. General Microbiol.* 1958, Oct., v. 19, No. 2, 289–97, 2 figs. on pl. & 1 text fig. [21 refs.]

These authors from the Israel Institute of Biological Research have found that *Pasteurella pestis* produces a substance which inhibits the growth of *P. pseudotuberculosis*: this they refer to as pesticin. It was formed by 23 out of 24 strains of *P. pestis* examined. Its action could apparently be studied satisfactorily only in solid media; either the 2 organisms were cultivated in layers one above the other, or pesticin-containing broth culture supernatant was spotted on medium preseeded with *P. pseudotuberculosis*: inhibition in liquid media was observed "but no quantitative results could be obtained". Pesticin is heat-labile and destroyed by trypsin. Ultra-violet irradiation of a 24-hour culture of *P. pestis* [which apparently contains no pesticin, although 48-hour cultures were the usual source of it] induces "pesticin biosynthesis" within 15 minutes at 37°C., maximum activity being reached in 2 hours.

L. P. Garrod

BROCK, T. D. **The Effect of Salmine on Bacteria.** *Canadian J. Microbiol.* Ottawa. 1958, Apr., v. 4, No. 2, 65–71. [16 refs.]

Salmine is a protamine obtainable from salmon sperm, containing arginine with small amounts of valine, serine and proline. Its action on bacteria was thought to be of interest because of its structural resemblance to polypeptide antibiotics such as polymyxin. Bacteriostatic action was studied with 15 bacterial species: concentrations varying from 8 to 12 μgm./ml. inhibited all Gram-positive species except *Streptococcus faecalis*, which was resistant: much higher concentrations were required for Gram-negative species except *Pseudomonas pyocyanea*, which was inhibited by 32 μgm./ml. Salmine was also bactericidal in water but not in broth. Other effects studied were agglutination, and an increase in turbidity produced under some conditions in suspensions of Gram-positive as well as Gram-negative bacteria. It is believed that salmine may be a useful tool in studies of the nature of the bacterial cell surface.

L. P. Garrod

ARU, L. Azione *in vivo* della D cicloserina sugli enterobatteri. [**Action of D Cycloserine on Enterobacteria**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1958, Oct., v. 39, No. 10, 603–15, 6 graphs.

The English summary appended to the paper is as follows:—

"The action 'in vivo' of D Cycloserine on enterobacteria was studied in six individuals. Qualitative and quantitative modifications of the fecal flora were seen. While the drug given in doses not higher than 500 mgr. pro die can exert either an inhibitory or a stimulating action on the intestinal flora, when given in doses of 750 or 1000 mgr. it can induce more or less rapidly a general diminution, sometimes intense, of the enterobacteria. A periodical examination of the feces should then be advisable in the patients treated by this drug."

SCHNITZER, R. J., DELORENZO, W. F., GRUNBERG, E. & RUSSOMANNO, R. **Chemotherapeutic Studies with 2,4-Dimethoxy-6-Sulfanilamido-1,3-Diazine (Madribon).** *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 421–4.

This paper by members of the staff of the Hoffmann-La Roche Co. in the United States gives brief particulars of the properties and antibacterial activity *in vitro* and *in vivo* of a new sulphonamide. Nothing is said about its clinical use or about most aspects of its pharmacological behaviour, except that its "half-life" in the blood of rats is 48 hours: it therefore evidently belongs to the long-acting class of this group of drugs. *In vitro*, staphylococci are highly sensitive to it and pneumococci and haemolytic streptococci much less so among Gram-positive organisms: among Gram-negative, *Escherichia coli*, *Klebsiella pneumoniae* and *Salmonella typhi* are highly sensitive, *Salm. paratyphi B* and *Salm. typhi-murium* moderately so, and *Pasteurella multocida* and *Pseudomonas pyocyanea* apparently resistant. Mice were inoculated intraperitoneally with these organisms, and treated with either a single dose or repeated doses for 4 days by the alimentary route. A single dose was almost as effective as repeated doses totalling the same amount. There are several wide discrepancies between *in vitro* and *in vivo* findings, notably in the susceptibility to treatment with only small doses of infections by organisms (*e.g. Str. pyogenes* and *P. multocida*) shown to be inhibited *in vitro* only by concentrations which these doses could not have produced in the body. *L. P. Garrod*

HIRSCH, J. G. **Bactericidal Action of Histone.** *J. Exper. Med.* 1958, Dec. 1, v. 108, No. 6, 925–44, 3 figs. [21 refs.]

These observations originated in work on phagocytin, an antibacterial substance obtainable from polynuclear leucocytes [this *Bulletin*, 1956, v. 31, 1051, 1143]. A change in the method of extracting this yielded another substance which proved also to be extractable from a variety of tissues and was identified as histone. Further studies were then conducted with calf thymus histone obtained from a commercial source. This was found to exert a fairly rapid bactericidal action in low concentrations (often <1 μgm./ml.) on *Escherichia coli*, *Shigella flexneri* and *sonnei*, *Salmonella typhi-murium*, *Pseudomonas pyocyanea* and *Staphylococcus albus. Staph. aureus*, *Salm. enteriditis* and *Streptococcus pyogenes* were resistant to 25 μgm./ml. Histone was found to be adsorbed to bacteria on which it had acted, the supernatant retaining little activity. Agar-grown organisms were less susceptible than those grown in broth. Histone was slightly more active in acid media. Its activity fell progressively in solutions of increasing ionic strength: various buffer salts permitted normal bactericidal action when in a concentration of 0·01 M, but inhibited it at 0·5 M; NaCl was even more inhibitory. Serum inhibited bactericidal action in neutral but very little in acid media; various other substances, including protamine, spermine, heparin and nucleic acid, were found to be inhibitory. Studies were also made of the dependence of bactericidal action on temperature and concentration [the results of which were as to be expected] and on bacterial numbers, with the interesting finding that about the same proportion were killed regardless of inoculum size. The relationship between histone and other antibacterial substances extractable from tissues is discussed. "The fact that susceptibility of many bacteria to killing by tissue basic proteins is markedly influenced by the composition of the test medium, may well account for some of the confusion and conflicting results in the literature dealing with antimicrobial action of cell extracts and tissue fluids." *L. P. Garrod*

COLLIER, H. O. J. & GRIMSHAW, J. J. **Local Action of some Antibacterial Substances against *Corynebacterium ovis* in Guinea-Pig Skin.** *Brit. J. Pharmacol. & Chemotherapy.* 1958, Sept., v. 13, No. 3, 231–7, 5 figs.

"When a suspension of living *Corynebacterium ovis* was injected intradermally in guinea-pigs, a lesion of roughly circular outline developed within 24 hr. Lesions of smaller diameter arose if benzylpenicillin, dequalinium, hedaquinium, cetrimide, or oxytetracycline were injected at the identical site, either before, with, or after *C. ovis*. Evidence has been obtained that such reductions of lesion diameter are due to direct action of drugs on bacteria and not to antitoxic or anti-inflammatory actions. Lesion diameters became less as drug dosage increased up to a limit, and these reductions provided a measure of local antibacterial action *in vivo*. Intradermal injection of higher concentrations of antibacterials, without *C. ovis*, produced comparable but somewhat flatter lesions, diameters of which increased with increasing concentration of drug and provided a measure of intradermal toxicity."

PRINDLE, R. F. **Practical Aspects of Interaction of Surfactants and Disinfectants.** *Soap.* New York. 1958, Nov., v. 34, No. 11, 81–9, 178, 3 figs.

This paper by a member of the staff of Lehn and Fink Products Corporation reports no new work: it is a review of the factors which have to be taken into consideration in formulating a phenolic disinfectant. A "surfactant" is a substance used for the "dispersion" or "solubilization" of a phenol compound of low solubility. [The paper contains a further addition to the jargon of this subject: reference is made to requirements for a disinfectant used for "janitorial" purposes. A janitor being simply a doorkeeper, a definition of this term would have been helpful.] 4 factors are discussed, the first being the nature of the active ingredient: the relative activity of phenol,

cresols, xylenols and various chlorinated compounds is specified. The surfactant may be a soap, and a disinfectant made with castor oil or coconut oil soap may be 3–4 times more active than one made with peanut oil or "tall" oil soap. Alternatively it may be synthetic: the substance of this class on which further discussion is based is alkyl aryl sulphonate. The 2 factors here considered are surfactant-phenolic ratio, which in the example given should not exceed 3 :1, and the effect of *p*H, which is towards greater activity on the acid side throughout the range *p*H 10·5–3·5. Some concluding remarks are concerned with cost, packaging and market appeal. *L. P. Garrod*

PUBLIC HEALTH LAB. SERVICE. Committee on Formaldehyde Disinfection [WILSON, G. S., Chairman]. **Disinfection of Fabrics with Gaseous Formaldehyde.** *J. Hygiene.* 1958, Dec., v. 56, No. 4, 488–515, 7 figs. [27 refs.]

This important paper reports the results of a collaborative study begun in 1950, some of the experiments in which were done in 6 different laboratories. The purely laboratory work was done largely with bacteria dried on cotton threads, exposed to formaldehyde vapour and cultivated without any attempt to disperse the bacteria and then enumerate survivors: quantitation was achieved by contaminating the threads with a series of dilutions of culture. By exposing these threads in jars containing formaldehyde solutions, studies were made of the effect of concentration, humidity (controlled by adding different salts to the solution) and temperature. Relative humidity above 58% accelerated disinfection, with some suggestion of an optimum at 80–90%. Temperature in the range 0–30°C. appeared to have little effect. [There appears to have been a good deal of variation between the results in different laboratories, and the authors regard this as inevitable, *i.e.*, as a result of "a real irregularity in the action of formaldehyde vapour".] Most of these tests were done with a micrococcus dried in a weak gelatin solution. When it was dried in serum, disinfection was more difficult. Some tests were also done with tubercle bacilli, *Bacillus subtilis* and variola virus, and the conditions required for destroying these organisms were calculated.

Further experiments were done to ascertain penetrating power. In one series of these the threads were placed in a perforated box wrapped in 3 or 15 layers of blanket which was exposed in a chamber: the disinfection of these was much delayed. 3 actual disinfectors were also used, a small one built in the laboratory, a commercial type in which heated formaldehyde solution was discharged into the chamber "as a vapour spray", and a large autoclave into which formalin was admitted after drawing a partial vacuum: the jacket temperature of this was such that the chamber atmosphere attained 100°C. Exposed threads in these disinfectors were usually sterilized but when under pillows or layers of blankets they were usually not, except in the autoclave, where an effect was sometimes obtained even beneath 28 layers of blanket. The authors are uncertain how much of this effect was due to heat as such, but they found in separate experiments that heat reduces the amount of formaldehyde absorbed by wool, and conclude therefore that it should aid penetration.

The general conclusion reached is that disinfection by formaldehyde vapour is unreliable and should be used "only when no other method is available". Bed coverings should be treated in other ways, mattresses enclosed in impervious covers which can be treated with liquid disinfectants, and "objects made in occupational therapy departments of tuberculosis hospitals ought to be of a material that can be sterilized by heat or immersion". *L. P. Garrod*

HOFFMAN, R. K. & WARSHOWSKY, B. ***Beta*-Propiolactone Vapor as a Disinfectant.** *Applied Microbiol.* Baltimore. 1958, Sept., v. 6, No. 5, 358–62, 3 figs.

β-Propiolactone has hitherto been used as a liquid germicide: these investigators of the U.S. Army Chemical Corps, Fort Detrick, Maryland, have tested it as a vapour, the test organisms being spores of *Bacillus subtilis* var. *niger* and *Staphylococcus aureus* dried on pieces of fabric and subsequently washed off and enumerated in culture. The results of the experiments with the former are presented in detail in graphs showing the effects of varying the concentration, temperature and relative humidity. The spores were very rapidly killed by a concentration of 1·5 mgm. per litre provided that the relative humidity was 75% or more: at lower humidities the action was much slower. A rise of temperature accelerated bactericidal action, but this was also satisfactory at low temperature (*e.g.*, 6°C.) at which other gaseous disinfectants are relatively ineffectual. Staphylococci were more susceptible than *B. subtilis* by a factor of only 4 or 5. A 2-storey building with a capacity of 50,000 cubic feet was maintained at a temperature of 24°C. with a relative humidity of 80% and 16 litres of β-propiolactone were disseminated in it as an aerosol. 2 hours later 55 cultures from areas contaminated with *B. subtilis* spores were all negative.

The authors estimate that β-propiolactone is 25 times more active than formaldehyde and 4,000 times more than ethylene oxide. It is reasonably non-toxic, clears more quickly than formaldehyde and has not been found to damage any materials. On the other hand it lacks the penetrating power of ethylene oxide and requires an inconveniently high humidity. It is not regarded as superior to ethylene oxide, but as probably better than formaldehyde for any purpose for which that is now used. *L. P. Garrod*

WRIGHT, Eleanore S. & MUNDY, R. A. **Studies on Disinfection of Clinical Thermometers. I. Oral Thermometers from a General Hospital.** *Applied Microbiol.* Baltimore. 1958, Nov., v. 6, No. 6, 381–3.

These authors criticize previous studies of thermometer disinfection as having been conducted by inappropriate methods. [It is true that to dry broth cultures on them is artificial, but workers who have used sputum do not deserve this stricture. These authors say "it is unlikely that sputum would be found on oral thermometers after use", but even if sputum be defined only as bronchial secretion, its main constituent, mucin, is also that of saliva.] The mercury was removed from clinical thermometers (and the end re-sealed) so that

they could be sterilized by heat. They were then placed in patients' mouths, left to dry for 3–4 hours, completely immersed in disinfectant solutions for 15 minutes, washed, and cultivated in broth. Organisms found were classified as streptococci (considered as most significant evidence of failure to disinfect), other Gram-positive cocci, Gram-positive and Gram-negative bacilli and yeasts. A series of tests was done with sterile thermometers, with distilled water instead of disinfectant solution to determine the accidental contamination rate (2%) and allowance was made for this in interpreting results. Either 50 or 100 tests were done with all disinfectants. Regular sterility was obtained with 2 phenolic disinfectants, with 70% (v/v) but not 50% ethyl alcohol, 10% formalin, and 0·1% benzalkonium chloride in 50% alcohol but not in water. 2 "iodophors" (iodine solubilized with nonionic detergents) also failed. The authors are now studying "the disinfection of thermometers used by patients with active pulmonary tuberculosis", and promise a further report on this. [It will not be surprising if in this study they are driven back to the use of sputum after all.] *L. P. Garrod*

BRIDENBAUGH, L. D. & MOORE, D. C. **Is Heat Sterilization of Local Anesthetic Drugs a Necessity?** *J. Amer. Med. Ass.* 1958, Nov. 8, v. 168, No. 10, 1334–7, 3 figs. [14 refs.]

In August 1957 the authors sent a questionnaire to all the 121 hospitals in the state of Washington about the treatment given to ensure sterility of local anaesthetics. They received 101 (83·5%) replies, and these showed that only 33 hospitals were autoclaving the drugs; the remaining 68 used various chemical solutions to disinfect the outside of the container. Only 2 hospitals were autoclaving the multiple-dose rubber-stoppered vials or bottles containing the local anaesthetic solutions used for such procedures as infiltration, field block, caudal block, epidural block or peripheral nerve block. The remaining 99 hospitals used these multiple-dose vials and bottles as received from the suppliers.

Since 1953 the authors have kept records of 17,368 regional block procedures done with local anaesthetic solutions autoclaved at 18–22 lb. per square inch for 30 minutes—*i.e.*, at temperatures around 126°C. (260°F.). They state that all the solutions examined [a list is given] could be so treated at least once without any evident reduction in their expected clinical effect although they would suffer some loss of potency. More than one or two such sterilizations might cause marked reduction in potency. Their 17,368 records contained no example of infection or neurological sequelae in any of these cases which could be blamed on the use of unsterile equipment or contaminated anaesthetic.

They strongly advocate that autoclaving should become the rule for all such solutions because of its reliability; because solutions may be contaminated through undetected cracks in the containers; because autoclaving of the local anaesthetic in its container greatly simplifies the preparation of anaesthetic trays; and because it may be or become a medico-legal necessity in the light of a court decision in Great Britain [see *Brit. Med. J.*, 1953, v. 2, 1165 and 1954, v. 1, 940]. *J. W. Howie*

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order: General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus; Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes, Leptospira; Anaerobes; Bacillus; Others.

COHEN, H. H. **Mutual Linkage between the Components in IX and XII in** *Salmonella typhi* **O-Antigen.** *J. Immunology.* 1958, Dec., v. 81, No. 6, 445–51, 9 figs. [19 refs.]

The object of the investigation described in this paper was to examine by immuno-chemical methods the O-antigen factors, IX and XII, present in the intact typhoid bacillus and to determine their proportionate representation in the organism. Using the classical strain *Salmonella typhi*, O 901, Cohen prepared, after the method of WEBSTER, SAGIN, LANDY, and JOHNSON [this *Bulletin*, 1956, v. 31, 324] a purified lipo-polysaccharide complex, which, however, still contained about 3% N. This antigen was then tested, untreated and treated with 0·02N NaOH, against an absorbed serum containing antibody only to O-factor IX and also against a IX,XII serum by quantitative precipitation and agar-gel diffusion techniques.

In the double agar-gel diffusion test it was possible to demonstrate at least 2 antigen components, but after treatment with alkali the lipo-polysaccharide appeared to have lost some of its ability to precipitate antibody and gave only one line in the agar-gel test but retained its ability to react with both IX and XII antibody. This result suggested that the antigen apparently destroyed by the alkali was neither the IX nor the XII fraction, but probably the protein.

Precipitation of the alkali-treated antigen with an absorbed serum containing only IX-antibody removed all the XII as well as the IX-antigen. Further, both antigenic components were demonstrated in the precipitate formed by the interaction between the lipo-polysaccharide and an antiserum specific for a single component. The author brings forward additional evidence to support his thesis that factors IX and XII, present in the purified lipopolysaccharide of *Salm. typhi* O 901, are so closely bound together that they probably exist in the same molecule. *H. J. Bensted*

PAOLETTI, A. & BUONINCONTRO, Luciana. Velocità di scomparsa dal torrente circolatorio di conigli normali ed immuni del vaccino tifico marcato con P^{32} ed iniettato par via endovenosa. **[Disappearance Rate of Typhoid Vaccine labelled with ^{32}P and inoculated by Intravenous Route from the Circulation of Normal and Immune Rabbits]** *Ann. d. San. Publica.* 1958, Sept.–October., v. 19, No. 5, 1019–31, 2 graphs. [16 refs.] English summary.

The vaccine was made from *Salmonella typhi* 501 and marked with ^{32}P from the radio-chemical centre at Amersham. 29 rabbits were used, in 2 batches of 14 and 15, the former acting as controls. After immunization of the second group both batches received 1 cc. of

marked vaccine per kgm. Blood was then taken at 1-minute intervals up to 5 minutes, then at 10 and 30 minutes, when the animals were killed. Portions of lungs, liver, spleen, kidneys and blood were tested with a Geiger counter.

The results showed that the marked vaccine disappeared more quickly and more completely from the immunized rabbits; the lungs showed the greatest radioactivity per gm., but the liver took up the greatest amount of antigen. After 30 minutes antigen had almost entirely disappeared from the blood. It was not possible to determine whether the antigen found in the lung remained there and was phagocytosed locally or whether after a delay it passed to other organs to be dealt with. *W. K. Dunscombe*

Peso, O. A. & Lebrum, J. F. Técnicas rapidas para el estudio de propiedades, bioqúimicas bacterianas. Su applicación en la investigación de enterobacterias patógenas. **[Rapid Methods for Studying Biochemical Properties of Bacteria. Their application in the Detection of Pathogenic Intestinal Bacteria]** *Rev. Obras San. de la Nación.* 1957, Jan.–Feb.–Mar., v. 21, No. 170, 19–23. [16 refs.]

Before adopting a method for investigating pathogenic or potentially pathogenic bacteria, the bacteriologist is faced with the problem of selecting it from 3 points of view, accuracy, speed and simplicity. In general the first 2 factors are mutually opposed. Very often in an attempt to attain great accuracy the final result is so long delayed that its practical value is lost; at other times accuracy has to be sacrificed in order to obtain quicker results. As for simplicity, there is no doubt that this factor is of fundamental importance when selecting routine techniques.

A medium is described for the rapid differentiation of suspect colonies and is made up as follows:—

(a) A basal medium:

Meat extract	6·00 gm.
Proteose-peptone No. 3	20·00 gm.
KH_2PO_4	2·00 gm.
NaCl	10·00 gm.
Bromo-thymol-blue (Soln. 1·6%)	10·00 ml.
Andrade indicator	30·00 ml.
Distilled water to	1000·00 ml.

*p*H 7·0

(b) Aqueous solutions of lactose, saccharose and urea at 50%, sterilized by Seitz filtration.

(c) Agar for sealing:

Agar	1·00 gm.
Bromo-thymol-blue (Soln. 1·6%)	0·20 ml.
Andrade indicator	0·60 ml.
Distilled water to	100·00 ml.

The final medium was prepared at the time of use, by adding to each 5 ml. of the basal medium 1 ml. of each of the sterile solutions and also 2 ml. of physiological saline. Portions of 0·15 ml. of the medium were kept in 5 × 50 mm. tubes at 37°C. in a water bath until the moment of use. Inoculation was performed with material picked from pure colonies obtained from the different primary isolating media and a sufficient quantity of sealing agar was carefully poured down the sides of the tubes so as to form a cover about 3 mm. thick.

It was found that results could be obtained with this medium within a period of 6 hours' incubation at 37°C. Its practical application made it possible to eliminate 75% of the inoculated colonies.

Media and methods for investigating hydrogen sulphide and indole which revealed the production of these substances within 2 to 4 hours' incubation at 37°C. are also described.

[The reviewer has a verbatim translation of this paper should any reader desire to know further details of the methods.] *E. Windle Taylor*

Stehr, K. Beiträge zur Biologie der *Salmonella paratyphi* B. I. Mitteilung. Phagozytose der Riesenformen von Paratyphus-B-Bakterien, die unter dem Einfluss von LiCl bzw. Cs Cl entstanden sind. **[Contributions to the Biology of *Salmonella paratyphi B.* 1st Communication]** *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 3/4, 213–31, 9 figs. (2 coloured on pl.)

Various shapes and giant forms of *Salm. paratyphi B* are produced by addition of lithium chloride or caesium chloride to the culture media. Lithium chloride produces round forms, caesium chloride fibrous (thread) forms. The object of the experiments carried out by the author was to ascertain the response to phagocytosis by guineapig leucocytes of the giant forms and whether or not H and O antibodies rendered them more susceptible to phagocytosis.

He found that fresh active guineapig serum either alone or in combination with rabbit normal or immune serum had only a weak stimulating effect on phagocytosis of organisms of the parent stem from which the aberrant organisms were derived. The first generation of cultures in lithium or caesium were no more susceptible to phagocytosis than the parent stem. O and H rabbit sera had a marked acclerating effect on phagocytosis of organisms of the parent stem but cultures in lithium and caesium were phagocytosed in smaller numbers than others grown on ordinary agar. Exposure of the bacteria to various concentrations of Li and Cs *in vitro* before exposing to phagocytosis revealed that phagocytosis was restrained after high concentrations and approached the level of the control after exposure to low concentrations. The action of the salts was therefore on the organisms and not the phagocytes. Moreover, if the organisms are washed, after exposure to the action of the salts, phagocytosis is not inhibited. Immune H and O sera stimulated phagocytosis of the aberrant forms, but the fibrous forms produced by Cs were phagocytosed more rapidly than the giant forms produced by Li. *P. A. Clearkin*

McDonagh, V. P. & Smith, H. G. **The Significance of the Abattoir in *Salmonella* Infection in Bradford.** *J. Hygiene.* 1958, June, v. 56, No. 2, 271–9, 1 fig. [12 refs.]

In the 3 years 1954–6 6 salmonella types were frequently grown from material from the Bradford abattoir

and the chief source of the organisms was apparently healthy pigs. The most common serotypes were *Salmonella typhi-murium* and Salm. Derby. There was marked overcrowding of the lairages at this time, which followed the end of meat rationing, and there was probably considerable infection among the animals.

Human salmonella infections in Bradford during this period could be related to the abattoir findings, both in the serotypes encountered and in the case of *Salm. typhi-murium* in the phage types also.

It is suggested that the abattoir is the most important source of human infection and that the main reservoir of infection is pigs. Shortening the stay of animals in the lairages and reduction of overcrowding might considerably reduce the number of animals found infected at slaughter. *J. Nagington*

COLLARD, P. & SEN, R. ***Salmonella* Types isolated in Ibadan, Nigeria.** *Trans. Roy Soc. Trop. Med. & Hyg.* 1958, May, v. 52, No. 3, 283–7.

Between late 1955 and the end of 1956 180 salmonella strains were cultured from human sources, mainly hospital patients, in Ibadan, Nigeria. They comprised 68 serotypes which included 10 new types.

The most common were *Salmonella typhi* (32 strains) and Salm. Agama (18 strains). Only 6 strains of *Salm. typhi-murium* were grown. Salm. Agama is of interest in being grown from human subjects with gastro-enteritis. It is a common inhabitant of the alimentary tract of the agamid lizard. *J. Nagington*

COLLARD, P. & SEN, R. **Salmonellae isolated from Man in Ibadan.** *West African Med. J.* 1958, June, v. 7 (n.s.), No. 2, 91–6, 1 fig. [14 refs.]

Much of this information is given in the paper by the same authors, above.

LE MINOR, L., NÉEL, R., DELAGE, B. & DRÉAN, D. Un nouveau sérotype de *Salmonella*. [**A New *Salmonella* Serotype**] *Ann. Inst. Pasteur.* 1959, Jan., v. 96, No. 1, 106–7.

The English summary appended to the paper is as follows—

"Description of a new *Salmonella* serotype, *S. tanger*, isolated from a tortoise and possessing the formula: 1,13,23 : 1,6."

LE MINOR, L., DARRASSE, H. & CHARIÉ-MARSAINES, C. Trois nouveaux sérotypes de *Salmonella*. [**Three New *Salmonella* Serotypes**] *Ann. Inst. Pasteur.* 1959, Jan., v. 96, No. 1, 107–8.

The English summary appended to the paper is as follows:—

"Description of three new *Salmonella* serotypes, isolated at Dakar from a water-tank and from lizards: *S. ouakam* (9)46 : z_{29} :-, *S. camberene* 35 : z_{10} : 1,5 and *S. yoff* 38 : z_4z_{23} : 1,2."

BÖHLCK, Ingeburg. Ein neuer Salmonellatyp: S. Kiel (1,2,12 : gp). [**A New Salmonella Type: Salm. Kiel (1,2,12 : gp).**] *Arch. f. Hyg. u. Bakt.* 1959, Jan., v. 143, No. 1, 82–4.

REAVIS, R. W. & EWING, W. H. **Fermentation of Raffinose by Shigellae.** *Internat. Bull. Bact. Nomencl. & Taxon.* 1958, Apr. 15, v. 8, No. 2, 75–8.

1,263 shigella cultures were examined for their ability to ferment raffinose. All the *Shigella sonnei* strains and the majority of the *Sh. flexneri* strains fermented raffinose. The only consistently negative *Sh. flexneri* types were the mannitol-negative *Sh. flexneri* 4a (36 cultures) and *Sh. flexneri* 6 (141 cultures which included all known biotypes). Of the other 475 *Sh. flexneri* strains about 81% fermented raffinose, one-third of them within 1 day.

None of the 209 *Sh. dysenteriae* and 273 *Sh. boydii* strains, including several provisional serotypes, fermented raffinose. Raffinose fermentation is therefore of considerable value in the characterization of the shigella group.

Of 344 *Escherichia coli* strains examined only 17% fermented raffinose. This series included 268 anaerogenic non-motile biotypes of the Alkalescens-Dispar group. Only 14% of these fermented raffinose and none of the cultures of O antigen groups 1 (107 strains) and 2 (89 strains) did. This may prove of use in their differentiation from *Sh. flexneri*. *J. Nagington*

OSONO, T. **Mechanism of the Desoxycholate-Citrate Medium for the Isolation of Dysentery Bacilli. III. Roles of Desoxycholate (Part II).** *Japanese J. Microbiol.* 1958, July, v. 2, No. 3, 257–69, 1 fig. [Numerous refs.]

SĂSĂRMAN, A. TULPAN, G. & VULCAN, V. Contribution à l'étude de la variation de phase chez les *Sh. flexneri* Type 2a. [**Contributions to the Study of the Phase Variation of *Sh. flexneri* Type 2a**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, June, v. 17, No. 2, 309–18. [21 refs.]

The English summary appended to the paper is as follows:—

"The present study represents a continuation of Prof. Combiesco's work on the antigenic variation of *Sh. flexneri* under the influence of certain medium factors.

"After repeated passages on culture media with tissue extracts a phase variation of *Sh. flexneri* type 2a was obtained.

"Those variants were easily detectable by the morphological character of the colonies, but the modifications were not of the type of the S—R variant. The variants obtained, were biochemically identical and did not obviously differ as virulence and toxicity for the white mice.

"One of the variants, phase A was agglutinated by the specific serum like the initial strain, whereas the other variant, phase B was agglutinated only by the group serum. It results that the latter lost its specific

antigenic component representing the phase group of type 2a.

"Besides the loss of the specific component, the variant B lost also a component common to type 2a and to the variant y, probably identical to the one noted by RAUSS as type $VIII_2$.

"Phase B acquired group components inapparent in the initial strain, where they were probably masked by the presence of the specific antigen resembling the phase group of other types."

NISHIMURA, C., NAKAMURA, M., OFUCHI, R., IWAHARA, S. & NOZAKI, Y. **Chemical Studies on Endotoxins. II. Sugars and Amino Acids Analysis of Purified Endotoxin of** *Shigella flexneri* **2b.** *Japanese J. Microbiol.* 1958, July, v. 2, No. 3, 247–55, 4 figs. [22 refs.]

IKARI, N. S., ROBBINS, Mary L. & PARR, L. W. **Action of Colicines on** *Shigella boydii* **and on their Rough and Mucoid Variants.** *Proc. Soc. Exper. Biol. & Med.* 1958, May, v. 98, No. 1, 142–4, 2 figs.

When rough (R) or mucoid (M) variants of several *Shigella boydii* serotypes were tested in parallel with their smooth (S) parent strains for sensitivity to a series of colicines it was found that in all cases the S cultures were markedly more resistant.

Reversal of R and M to the S forms by growth in broth containing Kinetin (6-furfurylaminopurine) partially restored the colicine spectrum to that of the S parent, but complete restoration did not occur.

It is thought that the sensitivity of *Sh. boydii* to colicines depends, at least partially, on the somatic antigen and that differences in susceptibility between serologically identical strains may be simply due to differences in the amounts of somatic antigen they possess. *J. Nagington*

MCNAUGHT, W. & ROBERTS, G. B. S. **Enteropathogenic Effects of Strains of** *Bacterium coli* **isolated from Cases of Gastro-Enteritis.** *J. Path. & Bact.* 1958, July, v. 76, No. 1, 155–8, 3 figs. on pl.

This paper records what is basically an enquiry into the claims of DE *et al.* [this *Bulletin*, 1957, v. 32, 279] who found that when pathogenic strains of *E. coli* were injected into ligated loops of rabbit bowel, pathological changes were produced. In the present investigation, 27 strains of *E. coli* were employed; 4 of these were untypable strains from healthy babies and the remaining 23 were sero-specific strains from the following sources —16 from patients with gastro-enteritis (1 adult), and 7 from babies with no symptoms. The inocula (2 ml. of 24-hour peptone water cultures) were injected into 4–6 inches of ligated loops of small bowel in rabbits; 24 hours later the animals were killed and the loops examined. Of the 16 strains isolated from patients with gastro-enteritis, 13 produced definite pathological lesions, while only 1 of the 11 control strains (7 typable, 4 untypable) produced any significant histological change. The authors conclude that these findings are further evidence of the close association between sero-specific strains of *E. coli* and infant gastro-enteritis.

John S. Stevenson

TAYLOR, Joan, MALTBY, M. P. & PAYNE, J. M. **Factors influencing the Response of Ligated Rabbit-Gut Segments to Injected** *Escherichia coli.* *J. Path. & Bact.* 1958, Oct., v. 76, No. 2, 491–9, 8 figs. (7 on 2 pls.)

Recently, attempts have been made to assess the pathogenicity of type specific strains of *E. coli* by injecting cultures into ligated loops of small bowel of rabbits [DE *et al.*, this *Bulletin*, 1957, v. 32, 279, and MCNAUGHT and ROBERTS, above]. The investigation reported here consists of a series of experiments designed to discover the factors on which depend the production of standard, reliable and reproducible results in these ligated intestinal loop tests.

In most of the work a non-pathogenic strain of *E. coli* O111 B4 H12 and a pathogenic strain of O26B6 were used; inocula were standardized to an average viable count of 30,000 in 4 ml. of peptone water. The rabbits were killed 24 hours after injection and the loops examined—control, non-injected loops were included in the tests. Dilatation and inflammation of the loop were produced by the pathogenic O26 strain, but not by the non-pathogenic O111, but variable results at the outset resulted in the use of one strain of rabbit —males of the Copenhagen stock. It was found that when the animals were fed on their own accustomed diet (No. 18) they produced more reproducible results than were obtained with mixed rabbit strains. Variation of *p*H of the inocula from 6·2 to 8·2 produced no change in the results obtained—this is not in accord with De *et al.*, who stated that dilatation of the ligated gut only occurs with pathogenic strains if the *p*H of the inoculum is 8·4. It was further found that the age of the cultures used (from 24 hours to 7 days) did not alter the results, but that negative results were obtained with cultures of the pathogenic strain which had been heated at 100°C. for 30 minutes and with extracts of this strain produced by freezing and thawing. De *et al.* stated that they found no evidence of polymorphonuclear cell infiltration in their loops of gut, but in the present investigation dilatation of the gut was always accompanied by purulent inflammatory change, with polymorphs migrating through the epithelium into the lumen. *John S. Stevenson*

WELSCH, M. Production de "protoplastes" d'*Escherichia coli* sous l'influence de la glycine en milieu saccharosé. [**The Production of "Protoplasts" of** *Escherichia coli* **by means of Glycine in the Presence of Sucrose**] *C.R. Soc. Biol.* 1957, v. 151, No. 11, 1990–93. [15 refs.]

When a culture of *E. coli* which has been grown on nutrient agar for 7 hours is suspended in a solution of glycine and incubated at 37°C. for 3–5 hours the bacteria are transformed into spherical shapes 4–6μ in diameter. These rapidly lyse unless stabilized by the presence of 10% sucrose. The most suitable concentrations of glycine for the demonstration of the phenomenon are M and M/2 solutions, M/4 is less effective and M/8 or less has no action. The best solution is M/2 glycine and 10% sucrose.

The spherical forms can persist for several days at low temperatures but they disappear in 24–48 hours at

37°C. They are only gradually destroyed after transfer to distilled water and this lack of fragility suggests that they may not be true protoplasts. *J. Nagington*

BANERJEA, A. **Nucleic Acid Contents of** *Escherichia coli* **and their relation to Bacterial Dissociation.** *Ann. Biochem. & Exper. Med.* 1958, v. 18, No. 3, 97–100.

Estimations were made of the nucleic acid content of 16 strains of *E. coli* (11 known serotypes and 5 isolated from normal infants). It was found that the smooth forms of these organisms showed wide variations in deoxyribose nucleic acid (DNA) and ribose nucleic acid (RNA) content, but that these variations did not bear any relationship to the pathogenicity or non-pathogenicity of the strains examined. Further estimations of DNA and RNA were made on *E. coli* O111B4, O55 B5, O26B6 and O86B7 during the change from smooth to rough forms and both acids were found to be decreased in O11, O55 and O86, along with a decrease in protein. The protein content of O26 (rough) was slightly increased, DNA was stationary, and RNA was much reduced. *John S. Stevenson*

SUZUKI, K. & ONO, J. **Biochemical Heterogeneity of the Ribonucleic Acid synthesized by** *Escherichia coli B* **after Irradiation with Ultra-Violet Light.** [Correspondence.] *Nature.* 1959, Feb. 7, v. 183, 395–6, 2 figs.

YOSHIDA, A. & SEVAG, M. G. **Effect of Streptomycin on Phosphate and Nucleic Acid Metabolism of** *Escherichia coli. Arch. Biochemistry.* 1958, Sept., v. 77, No. 1, 31–40, 1 diagram.

HAUGAARD, N. **D- and L-Lactic Acid Oxidases of** *Escherichia coli. Biochim. et Biophys. Acta.* 1959, Jan., v. 31, No. 1, 66–72, 2 figs. [15 refs.]

SHEININ, Rose & MCQUILLEN, K. **Effect of Penicillin on induced Enzyme Formation in Normal Cells and Spherical Forms of** *Escherichia coli. Biochim. et Biophys. Acta.* 1959, Jan., v. 31, No. 1, 72–4, 2 figs. [11 refs.]

COHEN, G. N. & MUNIER, R. Effets des analogues structuraux d'aminoacides sur la croissance, la synthèse de protéines et la synthèse d'enzymes chez *Escherichia coli.* [**Effects of Structural Analogues of Amino Acids on Growth and Synthesis of Proteins and Enzymes in** *Escherichia coli*] *Biochim. et Biophys. Acta.* 1959, Feb., v. 31, No. 2, 347–56, 8 figs. [13 refs.]

MCAFEE, R. D. & NIESET, R. T. **Studies of Amino Acid Metabolism in** *Escherichia coli* **with ^{15}N.** *Biochim. et Biophys. Acta.* 1959, Feb., v. 31, No. 2, 365–71. [16 refs.]

YANOFSKY, C. **A Second Reaction catalyzed by the Tryptophan Synthetase of** *Escherichia coli. Biochim. et Biophys. Acta.* 1959, Feb., v. 31, No. 2, 408–16, 4 figs.

HERZENBERG, L. A. **Studies on the Induction of β-Galactosidase in a Cryptic Strain of** *Escherichia coli. Biochim. et Biophys. Acta.* 1959, Feb., v. 31, No. 2, 525–38, 5 figs. [28 refs.]

WORMSER, Eva H. & PARDEE, A. B. **Regulation of Threonine Biosynthesis in** *Escherichia coli. Arch. Biochemistry.* 1958, Dec., v. 78, No. 2, 416–32, 2 figs. [19 refs.]

HURWITZ, C., REINER, J. M. & LANDAU, J. V. **Studies in the Physiology and Biochemistry of Penicillin-Induced Spheroplasts of** *Escherichia coli. J. Bacteriology.* 1958, Dec., v. 76, No. 6, 612–17, 2 figs.

DEERING, R. A. **Radiation Sensitivity of Filamentous** *Escherichia coli. Biochim. et Biophys. Acta.* 1959, Jan., v. 31, No. 1, 11–19, 6 figs. [13 refs.]

"Filamentous forms of *Escherichia coli* B have been irradiated with 250 kV X-rays or 2652 Å ultraviolet. The ability of the filaments to form visible colonies was used as the assay for survival. The survival curves for the filaments were 'single-hit' for any length filament with either X-rays or ultraviolet. The relative radiation sensitivity to either of these radiations increased in proportion to the filament length."

SARKAR, J. K. & TRIBEDI, B. P. **Is** *Alcaligenes faecalis* **a Pathogen, Contaminant or Normal Intestinal Flora?** *Indian J. Med. Sci.* 1958, Dec., v. 12, No. 12, 999–1006, 1 fig. [17 refs.]

It will be recalled that NYBERG [this *Bulletin*, 1935, v. 10, 413] drew attention to the confusion that existed about Petruschky's organism; he found that many cultures labelled *Bacterium faecalis alkaligenes* were in fact actively motile vibrios indistinguishable from the *Vibrio alkaligenes* (LEHMANN & NEUMANN). The name *Bact. faecalis alkaligenes* should be reserved for the true bacillary form which is usually non-motile. Sarkar and Tribedi promise a further paper on a systematic study of their organism, but without an adequate description it can only be assumed in the paper under review that they are referring to the type commonly known as *Bact. faecalis alkaligenes.* Nevertheless it is of interest to note that they record that 25% of the cholera convalescents they examined were excreting *"Alcaligenes faecalis"*. The authors did not find their organism commonly in the stools of healthy individuals; they successfully ruled out contamination from their positive blood cultures and, in the main, base their claim for pathogenicity on the fact that over a period of 3 years and out of 1,960 consecutive blood cultures (presumably typhoid suspects) *"Alcaligenes faecalis"* was the sole organism isolated from 71 patients, all of whom were suffering from an enteric-like fever. They examined various strains isolated for pathogenicity by

the intraperitoneal mouse test, with and without mucin and by the intestinal loop test [De and Chatterjee, *Trop. Dis. Bull.*, 1954, v. 51, 581]. These results were not very convincing from the point of view of pathogenicity but the high proportion of isolations of "*Alcaligenes faecalis*" from blood cultures as the sole organism from patients with enteric-like fevers is impressive.

[The reviewer has frequently isolated *Bact. faecalis alkaligenes* in India from the blood of patients with a variety of fevers, but in most cases there was strong evidence for regarding the organism as a concomitant—the result of the condition rather than its cause. On several occasions it was isolated in conjunction with *Salmonella typhi* or *Salm. paratyphi A* from true cases of enteric fever or was present in the blood stream of patients suffering from scrub typhus and in all these instances the same organism was present in considerable numbers in the stools of these patients. Although it may well be that *Bact. faecalis alkaligenes* can initiate a true infective condition in man the evidence advanced in this paper is not sufficient by itself to accept the pathogenic role given to it.] *H. J. Bensted*

Lark, Cynthia & Lark, K. G. **Nucleic Acid Synthesis in Penicillin-treated** *Alcaligenes faecalis*. *J. Bacteriology*. 1958, Dec., v. 76, No. 6, 666–7, 1 fig.

Sedlák, J. & Matějovská, D. **On the Taxonomy and Systematics of the** *Aerobacter cloacae* **Groups (***Cloaca cloacae***).** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 3, 285–99. [32 refs.]

The authors examined 120 strains originally identified as *Paracolobacterium aerogenoides*. In the tests used there were 14 different "types" and one strain of each was used to prepare appropriate "type" antisera. Of the 14 cultures, one was later determined as *Bacterium anitratum*; the other strains were regarded as being typical (gelatin-positive) or atypical (gelatin-negative) *Aerobacter cloacae*. Later still, 2 of the gelatin-negative strains were redetermined as atypical members of the Citrobacter and Arizona groups respectively.

Those strains that the authors accepted as *Aerobacter cloacae* were divisible by O agglutination into 8 groups. These O groups shared antigens with members of other groups of the family Enterobacteriaceae; *e.g.* O group 1 had antigens in common with *Salmonella onderstepoort* and with Providencia.

Of the biochemical tests the authors found useful those for indole, H_2S, KCN, mucate, decarboxylases and phenylalanine. They did not regard the results of the MR and VP tests as satisfactory or significant in classification. *S. T. Cowan*

Mandel, P. Terranova, T., Sensenbrenner, M. & Feo, F. **Oxygen Consumption of Different Forms of Stable L** *Proteus* **P 18 growing in Hypertonic Liquid Medium.** [Correspondence.] *Nature*. 1959, Jan. 17, v. 183, 194–5, 3 figs.

Pope, C. G. & Stevens, Muriel F. **The Properties of Crystalline Diphtheria Toxin-protein: Observations on the Phosphate-Stable antigen.** *Brit. J. Exper. Path.* 1958, Aug., v. 39, No. 4, 386–92, 3 figs.

The authors continue their intimate analysis of crystalline diphtheria toxin of high potency [this *Bulletin*, 1958, v. 33, 876] prepared by special methods. They have already described [*ibid.*, 1958, v. 33, 877] the modification of these preparations by exposure to K_3PO_4 and the apparent increase in Lf value of the toxin which results.

In further investigations the optical density of toxin-antitoxin mixtures in which the amount of antibody is constant and the toxin is progressively increased is observed. These observations show that the effect of K_3PO_4 treatment is to promote the appearance of a K_3PO_4-stable antigen which flocculates earlier, *i.e.* in combination with a greater proportion of antibody than the original crystalline toxin protein. Simultaneously, there is a marked loss of skin reacting toxin which can be demonstrated in animal tests. *J. W. McLeod*

Pope, C. G. & Stevens, Muriel F. **The Properties of Crystalline Diphtheria Toxin-Protein: Observations on the Pepsin and Trypsin-Stable Antigens.** *Brit. J. Exper. Path.* 1958, Oct., v. 39, No. 5, 490–96, 2 figs. [10 refs.]

In further pursuit of their work on the composition of crystalline diphtheria toxin, the authors have examined by optical methods the curves obtained by mixing progressively larger amounts of pepsin-digested toxin with a constant amount of antibody. They have used digests of toxin at *p*H 3·7 and 4·7.

The product of digestion at 4·7 shows evidence of 2 optima for flocculation, one with slight excess of antibody and the other with considerable excess of antigen. This preparation gives 4 lines on gel-diffusion plates with pepsin-refined antitoxin. The presence of the antigen flocculating with excess of antibody is still clearly shown in the curves obtained with the product of digestion at the lower *p*H.

Further investigation of the crystalline toxin preparations has shown that the trypsin-resistant antigenic complex first demonstrated in toxin of lesser purity in 1951 [Pope & Stevens, this *Bulletin*, 1952, v. 27, 295] may also be present in crystalline toxin but irregularly since its appearance is dependent on the method of preparation of the crystalline toxin. It is specially liable to appear in preparations obtained by ultrafiltration. In contrast with the peptic digestion and K_3PO_4-resistant antigens, this antigen resistant to tryptic digestion gives maximum flocculation when moderately in excess of antibody.

It is claimed therefore that 3 distinct antigens have been shown to be present in crystalline diphtheria toxin, none of which is identical with the specific toxin of the *Corynebacterium diphtheriae* and which constitute what the authors describe by the term "flocculation envelope" of the specific toxin titrated by the Ramon flocculation technique. *J. W. McLeod*

SALL, T., MUDD, S. & TAKAGI, A. **Polyphosphate Accumulation and Utilization as related to Synchronized Cell Division of** *Corynebacterium diphtheriae*. *J. Bacteriology*. 1958, Dec., v. 76, No. 6, 640–45, 14 figs. [15 refs.]

EYLAN, E. & ISRAELI-FURMANOW, E. **The Cultivation of** *Mycobacterium tuberculosis* **on Millipore Filters.** *Harefuah*. Jerusalem. 1958, June 15, v. 54, No. 12, [in Hebrew 305–8, 2 figs. (15 refs.) English summary 308–9].

The technique is to treat the sputum or other material with NaOH in the usual way, neutralize, and shake for 20 minutes in 15% trisodium phosphate solution, and pass the material through a millipore filter No. 5, under vacuum. The filter is then placed on Löewenstein-Jensen medium in a Petri dish and incubated in a moist atmosphere. Round smooth colonies appear on the filters after 3–5 days of incubation and can be stained with neutral red.

The filter method was compared with the ordinary method of direct cultivation on the same medium. 64 samples were tested, and the filter method gave 68·7% of positive results, against 35·9% by direct culture. Moreover, the colonies appeared much more quickly by the filter method.

Acid-fast saprophytes grow well in this way, and can easily be distinguished from tubercle bacilli by the fact that the cultures stain brown-yellow with neutral red, grow more quickly than tubercle bacilli, and are coloured. *Charles Wilcocks*

LENERT, Tulita F., STASKO, Irene & HOBBY, Gladys L. **The Cultivation of the Bacille-Calmette-Guerin Strain of** *M. tuberculosis* **(BCG).** *Amer. Rev. Tuberculosis*. 1958, Dec., v. 78, No. 6, 934–8, 1 fig. [Refs. in footnotes.]

This note describes a medium which enables large numbers of BCG suitable for the development of cell-free preparations for immunizing against tuberculosis to be grown in 14 days. 31 modifications of Sauton, Long and Dubos media were investigated, and crude reagents were found to be less satisfactory than CP [chemically pure] or USP [United States Pharmacopoeia] chemicals; sodium glutamate was superior to asparagine, ammonium succinate, N–Z Case (Sheffield) or ammonium phosphate, and glycerol was superior to glucose.

Incubation was for 14 days on a rotary shaker and the yield of acetone-washed and air-dried or water-washed and lyophilized, phenol-killed bacilli was 9·1–28·8 (average 19·45) gm. per litre of medium. Some of the bacilli were single but the majority were closely bound in parallel formation; they were elongated, slender and pale staining, but they grew typically when they were sub-cultured on oleic-acid-albumin agar.

The Phipps strain of BCG was used for this study and mice infected intravenously with approximately 13×10^6 cells usually died within 48 hours whereas mice infected with a similar number of normally grown bacilli survived for a period of 119 days; an inoculum of $1{\cdot}3 \times 10^6$ of the shaker-grown bacilli was not lethal. This apparent increase in virulence may be due to the presence of dead bacilli for not all the cells in the culture were viable and other workers have shown that dead BCG can cause an apparent increase in the virulence of staphylococci [this *Bulletin*, 1958, v. 33, 270]. *S. R. M. Bushby*

HOBBY, Gladys L., LENERT, Tulita F. & STASKO, Irene. **The Biologic Activity of Crude Extracts of BCG.** *Amer. Rev. Tuberculosis*. 1958, Dec., v. 78, No. 6, 939–43, 3 figs.

The experiments described in this paper show that BCG grown *en masse* in the medium described in the above paper affords protection against tuberculosis when injected as phenolized-killed bacilli or as a crude extract. The experiments were done in mice and the Vallée strain of tubercle bacilli was used as the challenge.

Protection by the intact cells was shown by an increase in the survival time and this was more apparent with 0·3 mgm. than with 1·0 mgm. of BCG. Greater protection was, however, afforded by filtrates of cells ruptured by sonic vibration, and this protection was further enhanced if whole cells or extract were given in Freund's adjuvant, although the increase with Freund's adjuvant was no greater than that obtained by giving 2 doses of the immunizing agent without adjuvant. Some non-specific protection was afforded by the intact bacilli against pneumococcal and staphylococcal infections, a property of BCG vaccination that has been reported by other workers [this *Bulletin*, 1958, v. 33, 270]. *S. R. M. Bushby*

SCHELLENBERG, Hildegard. Tuberkelbakterien in HeLa-Zellen und anderen Geweben. [**Tubercle Bacilli in HeLa and Other Tissue Cultures**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 339–54, 29 figs. [18 refs.]

A variety of mycobacteria of graded virulence were investigated including the H37Rv strain as fully virulent, the H37RvIr strain as an organism of lower virulence and *Mycobacterium smegmatis* as an example of a saprophytic form. These were grown in cultures of HeLa cells of rat sarcoma cells, and fowl and rat fibroblasts. The growth rates of the cell cultures infected with highly virulent strains and with less virulent or avirulent strains have been compared as well as the variations in the morphological appearances of such cultures.

It is found that the growth of cell cultures is markedly reduced in the presence of the virulent forms and that the mycobacteria tend to appear in dense cords after a few days and sometimes surround the nuclei.

With forms of reduced virulence and saprophytic bacteria the tumour or tissue cells grow much better and the bacteria appear as small circular colonies or loosely assembled masses.

These differences are most marked in HeLa cell cultures and are adequate for distinguishing between virulent and avirulent strains of *Myco. tuberculosis*.

J. W. McLeod

YAMADA, S. **[Studies on the Influence of the Antituberculous Drugs contained within Samples on the Cultivation of the Tuberculous Bacilli]** *Igaku Kenkyu.* Fukuóka. 1958, Apr., v. 28, No. 4, 1143–70, 18 figs. [114 refs.] [In Japanese.] English summary.

The author attempted to cultivate tubercle bacilli from sputa positive on microscopic examination and from specimens of resected lung tissue, also microscopically positive. The materials were from patients undergoing treatment with streptomycin, isoniazid, PAS or "SI" [which is not explained] and a high proportion of attempts at cultivation failed. He found that the highest concentration of these drugs in the sputum occurred 1–3 hours after administration, and approached or even passed the lethal concentration for tubercle bacilli; moreover, there was cumulative action with multiple drug therapy.

The author therefore recommends cessation of administration of drugs for 1 day or more before cultivation of tubercle bacilli from sputum is attempted.

Charles Wilcocks

PENIKETT, E. J. K. & LISTER, A. J. **Estimation of Hydrogen Peroxide in Culture Media.** [Correspondence.] *Nature.* 1958, June 14, v. 181, 1682.

Small quantities of hydrogen peroxide produced in culture media, and also by some antituberculous substances, are thought to have an inhibitory effect on catalase-negative strains of *Mycobacterium tuberculosis* resistant to isoniazid. The authors report an indirect polarographic method which is sensitive in estimating peroxide, and which depends on the measurement of oxygen released from hydrogen peroxide by the action of catalase.

"10-ml. samples of media to be tested are freed of oxygen by the passage of nitrogen. Six units of Worthington catalase are added, and the oxygen-diffusion current measured at −0·50 V. with a recording polarograph, using a mercury dropping electrode and a saturated calomel half-cell and agar bridge. A standard curve of oxygen-diffusion current against peroxide concentration is constructed for each batch of media. The unknown concentration of peroxide is found by entering the oxygen-diffusion current in the standard curve. When only occasional observations are required Hohn's method of standard addition can be used."

Charles Wilcocks

ŠOUREK, J. & ŠÍR, Z. Antigenní příbuznost nativních filtrátů kultur některých zástupců mycobacteriales. **[Antigenic Relationships between Native Culture Filtrates of some Representatives of Mycobacterials]** *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 1, 33–41, 4 figs.

The English summary appended to the paper is as follows:—

"Mutual antigenic relations amongst the species of the genera Mycobacterium, Streptomyces and Nocardia have been investigated by an immunochemical analysis of specific precipitation in agar for which native culture filtrates have been used. On the basis of the results obtained, Mycobacteria are divided into two groups.

"I. The first group includes Mycobacterium tuberculosis var. hominis, bovis and muris ($H_{37}Rv$, VR, $H_{37}Ra$, Ravenel, BCG, MP).

"II. The second group consists of saprophytic Mycobacteria (M. phlei, M. smegmatis, M. saprophyticum) and of atypical Mycobacteria (strains 'V. S.' and 'R. W.').

"Mycobacterium avium, Streptomyces griseus and Nocardia asteroides cannot be placed in any of the two groups on the basis of their reactions. Their mutual relations have not been investigated any further.

"The method of specific precipitation in agar for which antigens prepared in the way described in this paper have been used has failed to differentiate between the virulent and the vaccine human and bovine strains. The vaccine strains BCG and MP do not differ essentially in their antigens from the virulent strains. The atypical strains 'R. W.' and 'V. S.' seem to represent a connecting link between the first and the second group and Streptomyces. Streptomyces preserves its weak antigenic relation to the first group. Nocardia excludes itself entirely from any antigenic relationship. Mycobacterium avium does not react with antibodies of the second group to which it belongs, but it reacts with $H_{37}RV$ and BCG of the first group, OT reacted almost with all the antiserums used.

"In the course of the adsorption and denaturation processes, it is the reaction with the protein antigens which disappears first, before the reaction with the polysaccharides.

"It follows from our results obtained so far that the method described above of employing complex culture filtrate tuberculins is not fit for the discrimination between the virulence of, or for the typing of, Mycobacterium tuberculosis (var. hominis-bovis-muris) strains."

GILANI, S. & SELKON, J. B. **The Niacin Test for Differentiating Human Tubercle Bacilli from other Mycobacteria.** *Tubercle.* 1958, Dec., v. 39, No. 6, 396–8.

Several workers have shown that human tubercle bacilli produce more niacin (nicotinic acid) than bovine tubercle bacilli [this *Bulletin,* 1957, v. 32, 897]. In the present paper the authors claim to have successfully modified the method of KONNO, KURZMANN, BIRD and SBARRA [*ibid.,* 1958, v. 33, 983] so that it can be used with ease on large numbers of cultures.

In the trial of the method the bacilli were grown on 7H–10 oleic-acid-albumin agar medium because the malachite green in Löwenstein-Jensen medium interferes with the test. Several tubes of medium were inoculated with about 0·01 mgm. of each strain and incubated at 37°C. and at intervals 1 ml. of 10% cyanogen bromide solution in water, which was stored in a dark bottle in the refrigerator and prepared each 14 days, was poured over the growth and 5 minutes later 1 ml. of 4% redistilled aniline in ethanol, which was also stored in the refrigerator, was added. The presence of a yellow colour in the fluid was recorded as positive, and the

residual cyanogen bromide, which liberates toxic fumes, was destroyed by adding 10% ammonia. The pigment of the chromogenic mycobacteria did not interfere with the test because it did not diffuse from the bacilli.

Of the 8 virulent, 4 attenuated isoniazid-resistant and one H37Ra strains of human tubercle bacilli examined, all gave positive reactions after 5–8 weeks' incubation although some gave a positive reaction after 3 weeks. Of 5 bovine strains, 1 strain of *Mycobacterium avium*, 5 atypical acid-fast bacilli and 2 saprophytes, none gave a positive reaction. *S. R. M. Bushby*

MUROHASHI, T.; YOSHIDA, K. **A Method for the estimation of the Number of Colonies recoverable from Sputum based on the Number of Tubercle Bacilli detected on Smears. I. Estimation Formulas and Preliminary Test** [MUROHASHI & YOSHIDA]. *Acta Tuberculosea Scandinavica.* 1958, v. 36, Nos. 2/3, 173–8. **II. Simplification of the Method by the Use of Estimation Graph or Bacterial Count Table in order to determine the Dilution Degree for Quantitative Cultivation** [MUROHASHI & YOSHIDA]. *Ibid.*, 179–86, 3 figs. **III. Confidence Interval of the Estimated Viability** [MUROHASHI]. *Ibid.*, 187–94, 1 fig.

In the first of these papers the authors show that if a standard loop, made of wire of 0·7 mm. thickness and having an inner diameter of 3 mm., is used for making a smear of homogenized sputum spread over an area of 12 mm. diameter, and the smear is examined with an oil-immersion objective, with a field of 0·12 mm. diameter, the number of bacilli per field multiplied by 2×10^5 gives the number of bacilli present in 0·1 ml. of the homogenized sputum.

If the authors' malachite-green-fuchsin method [this *Bulletin*, 1958, v. 33, 387] is used for staining the smears, an estimate can be made of the proportion of viable bacilli present, but as only 20–80% of the green-staining bacilli grow when cultured, the number of viable bacilli in 0·1 ml. of the sputum should be assumed to lie within these limits. The validity of this assumption was confirmed by the viable counts obtained from 31 samples of sputum, for the counts from 50% of specimens fell within these limits of 20–80% of the green-staining bacilli.

In the second paper the authors present graphs, based on the total number of bacilli present in Ziehl-Neelsen-stained smears and on the green-staining bacilli in smears stained by the double stain, which are suitable for determining in daily practice the dilution necessary for quantitative cultivation. 58 specimens were examined by the 2 staining methods and the results plotted on the graphs show that the count of the green-staining bacilli gave the best agreement, especially when it is assumed that only 40% of these bacilli are viable.

In the third paper the results obtained with the 58 specimens of sputum and cells from suspensions of BCG are examined statistically. Comparison of the results of counting 20 and 50 fields shows that 20 fields are sufficient for routine use and an analysis of the standard deviations suggests that the distribution of the bacilli is that of a Poisson curve; the value of counting only the green-staining bacilli is confirmed.

The authors suggest that the method is of value for estimating the viability of murine leprosy bacilli.
S. R. M. Bushby

MUROHASHI, T. & YOSHIDA, K. **Improvement of Malachitegreen-Fuchsin Staining. A Differential Staining Method of Tubercle Bacilli.** *Acta Tuberculosea Scandinavica.* 1958, v. 36, Nos. 2/3, 195–8, 1 fig.

The original malachite-green-fuchsin staining method [this *Bulletin*, 1958, v. 33, 387], which was considered to stain viable bacilli a green colour owing to the state of polymerization of the DNA, is not always satisfactory for the staining of sputum.

In the improved method the smears, after heat fixation, are stained with 1% malachite green (*p*H 4·0) at 50–60°C. for 5 minutes and allowed to cool to room temperature. They are washed and stained with 1:10 carbol fuchsin (*p*H 5·6–6·0) for 5 minutes at 20°C. and decolorized and counterstained by immersion in a solution prepared as follows: 4 parts of 1% Bismark brown and 1 part 1% picric acid which has stood for several hours and is filtered; to 30 parts of the filtrate 100 parts of 2 % nitric acid are added.

Fair parallelism is claimed between viability and stainability to malachite green; microcolonies grown in submerged culture were composed mainly of green-staining bacilli. *S. R. M. Bushby*

GANCEVICI, G., PETROVICI, A. & DAVINDESCU, R. **Structural Details in Mycobacteria after Hydrolysis.** *Arch. Roumaines Path. Expér. et Microbiol.* 1958, June, v. 17, No. 2, 237–44, 13 figs. [13 refs.]

The English summary appended to the paper is as follows:—

"An insoluble specifically inert material, containing cell walls and electron-opaque volutin granules was isolated from Myco. tuberculosis $H_{37}Rv$ by the action of strong alkali hydrolysis followed by trypsin and formamide treatment.

"Electron micrographs and staining tests showed that the preparations were free from any soluble cellular material.

"Two different areas were observed in the metachromatic volutin granules."

VANDIVIERE, H. M., VANDIVIERE, Margaret R. & WILLIS, H. S. **Quantitative Studies of Virulence.** *Acta Tuberculosea Scandinavica.* 1958, v. 36, Nos. 2/3, 205–11. [15 refs.]

The method used in this study is based on that of HAN, KELLY and WOODRUFF [this *Bulletin*, 1954, v. 29, 353], in which a standard inocula of tubercle bacilli is injected intraperitoneally into guineapigs and 14 days later the weight in gm. of the omentum, which traps most of the bacilli, is divided by the body weight in kgm. of the animal; this figure is termed the omental index.

With an inoculum of 0·1 mgm. of 6 strains of tubercle bacilli grown for 14 days on Löwenstein-Jensen medium and having total viable units of $2·3–3·1 \times 10^6$ per inoculum, good correlation was found between the

omental indices and the duration of allergy produced by the strains and also their ability to "cord" in human plasma in varying concentrations of Tween 80. The strains and the indices were: $H_{37}Ra$, 0·4; 3 strains of BCG, 0·72, 1·18 and 1·85; R1Rv, 2·42; H37Rv, 6·90.

Similar indices were obtained with bacilli from Dubos medium, with inocula of 0·025 mgm. but not with 0·05 or 0·1 mgm.; with the larger inocula the omental response was disproportional. *S. R. M. Bushby*

GERNEZ-RIEUX, C., TACQUET, A. & GÉRARD, A. Action du B.C.G. sensible ou résistant à l'isoniazide sur la tuberculose expérimentale du lapin. Première partie. Influence sur l'évolution générale de la tuberculose. [**Action of BCG Sensitive or Resistant to Isoniazid on Experimental Tuberculosis in Rabbits. 1st Part. Influence on General Development of Tuberculosis**] *Ann. Inst. Pasteur de Lille.* 1957, v. 9, 7–22, 3 figs. [12 refs.]

In these experiments rabbits were infected intravenously with 0·001–0·01 mgm. of the Ravenel strain of the bovine tubercle bacillus and 14 days later the majority were vaccinated with BCG. The BCG was either the normal isoniazid-sensitive strain or an isoniazid-resistant variant of it; they were administered either orally, 75–900 mgm., or intradermally in weekly doses of 1 mgm. Those not vaccinated were given tuberculin injections instead.

In the first series of experiments, 490 mgm. of the parent strain of BCG was found to have a deleterious effect, for the animals died about 2 weeks earlier than control unvaccinated animals which died in 8–9 weeks; the vaccinated animals also lost more weight and showed more extensive disease. In another experiment, vaccination with the resistant strain was shown, however, to have the opposite effect, for the control animals died in 40 days, those vaccinated with the sensitive strain in 44 days and those with the resistant variant in 65 days; the weight loss and the extent of the disease were also relatively much less. The effects of the vaccination on the titre of the antibodies detectable by the Middlebrook and Dubos technique were also followed; vaccination with the parent strain caused a drop in titre but with the resistant variant there was initially a similar drop but this was followed by a rise. However, in neither series of these animals was there a significant difference in the number of bacilli recovered from the lungs.

In the second series of experiments the animals were treated after vaccination with a sub-minimal effective dose of isoniazid (1·5 mgm. per kgm. twice daily subcutaneously) and the results were very similar to those of the first series except that the number of bacilli recovered from the lungs of the rabbits vaccinated with the resistant-variant and treated with isoniazid was much reduced. In further experiments in which vaccination was by the intradermal route, the protective effect of the resistant BCG was again seen and the intradermal lesion produced by the organisms persisted longer than that of the parent strain.

In the experiment in which the animals were given 0·1 ml. of Old Tuberculin intradermally, the tuberculin had a very deleterious effect for although the animals survived a little longer than those not given the BCG, the loss in weight was greater and the lesions were more extensive.

Thus, under the conditions of these experiments, large doses of BCG given 14 days after infection aggravated the tuberculosis but similar doses of a resistant variant of the BCG diminished the effects of the infection and enhanced the activity of isoniazid; this variant was catalase- and peroxidase-negative. *S. R. M. Bushby*

GERNEZ-RIEUX, C., TACQUET, A. & MACQUET, V. Action des hormones corticoides sur l'infection tuberculeuse du cobaye et du lapin par les bacilles résistants à l'isoniazide [**Influence of Corticoid Hormones on Tuberculous Infection produced in Guineapig and Rabbit by Isoniazid-Resistant Tubercle Bacilli**] *Ann. Inst. Pasteur de Lille.* 1957, v. 9, 23–37.

In the first experiment, in which guineapigs were injected intradermally with a strain of tubercle bacilli resistant to 100 μgm. isoniazid per ml., the daily administration of 5 mgm. per kgm. of hydrocortisone, started either the day after infection or 18 days later, had no significant effect on the development or regression of the local lesion, on the spread to the glands and viscera, or on the multiplication of the tubercle bacilli in the cutaneous lesion or the draining lymph gland.

In the second experiment the effects of daily administration of 0·5 mgm. cortisone per animal on the lesion produced by a catalase-negative strain was determined. This strain was resistant to 5 μgm. isoniazid per ml. and was sensitive to 2 μgm. PAS and 1 μgm. streptomycin per ml. In one group of guineapigs the treatment with cortisone was started the day after the infection and continued for 40 days, when the animals were killed, and in another it was delayed till the 40th day and the animals were killed on the 80th day. The infection was again intradermal and the local lesions of the animals treated from the beginning were a little larger than the untreated ones, and whereas by the 80th day the lesions of untreated guineapigs had healed, those given the cortisone from the 40th day were still ulcerated. The treatment had no effect on the number of bacilli and there was no spread to the viscera.

In the third experiment the tubercle bacilli and the cortisone treatment were the same as in the second experiment, but the bacilli were injected subcutaneously. The treated animals gained a little less weight than the untreated ones, but there was no difference in the allergic state of the animals. In no animal did the infection spread to the lungs, and in only 1 was it present in the spleen; the lesions at the injection site and in the draining lymph gland were, however, larger in the animals treated after the 40th day than in the corresponding untreated group.

The fourth experiment was in rabbits infected with a variant of the Ravenel strain resistant to 300 μgm. isoniazid per ml. and catalase-negative. The bacilli were injected intravenously and the rabbits were treated with either 12·5 or 4 mgm. hydrocortisone per kgm. each day, starting the day after infection. The animals treated with the larger dose developed lipaemia and fatty degeneration of the liver and died of intercurrent

infection, their lungs contained more tubercle bacilli than those of the untreated control animals. In the animals treated with the lower dose of cortisone the number of tubercle bacilli present in the lungs was also greater than in the control animals and there were also renal lesions which were not seen in the control animals. *S. R. M. Bushby*

TACQUET, A. & GÉRARD, A., with the technical collaboration of R. WATTELLE. Rapport entre le délai d'apparition des cultures sur milieu a l'oeuf et la sensibilité de *Mycobacterium tuberculosis* aux substances antibacillaires. [**Relation between the Delay of appearance of Cultures on Egg-Medium and the Sensitivity of** *Mycobacterium tuberculosis* **to Antibacillary Substances**] *Ann. Inst. Pasteur de Lille.* 1957, v. 9, 38–47. [12 refs.]

This study was made on 1,159 strains isolated during 1956 and 841 during 1957 from pathological specimens treated with Teepol and caustic soda and cultured in 3 tubes of Löwenstein-Jensen medium and 1 tube of the same medium without glycerol. The cultures were examined every 15 days and discarded after 12 weeks' incubation. Sensitivity tests were done on the positive cultures, using Dubos medium.

The results of the analysis of the results are presented in tabular form and are classified as early positive, the tubercle bacilli growing in 21 days, and late positive. The cultures in the groups are also subgrouped according to the number of bacilli present in the original smear of the specimens, and according to their resistance to isoniazid, streptomycin and PAS. The table shows that of the total 2,000 positive cultures, 22·1% were late positives and that there was no significant difference between the various resistant strains. This figure is compared with that of 1951, when of 251 cultures, 31·5% were late positives; and the authors attribute this decrease to the change in the method of treating the specimens; in 1951 Petroff's method was used.

Comparison of the number of negative cultures from smear-positive specimens showed that they were increasing; in 1955, of the 966 positive specimens, 5·9% gave negative cultures, in 1956, of the 1,215 specimens, 5·1% were negative, and in 1957, of 916 specimens, 8·7% were negative.

The incidence of resistant strains to streptomycin and isoniazid was also greater in 1957 than in 1956 but not of strains resistant to PAS, the percentage of strains resistant to 10 μgm. streptomycin per ml. being 14·6% during 1956 and 18% during 1957, and for those resistant to 0·5 μgm. isoniazid per ml. being 38·6% during 1956 and 58·0% during 1957. *S. R. M. Bushby*

GUILLAUME, J., TACQUET, A. & PONTÉ, C. Interférence des acides aminés soufrés dans le dosage chimique de la cyclosérine. [**Interference by Amino Acids in the Chemical Estimation of Cycloserine**] *Ann. Inst. Pasteur de Lille.* 1957, v. 9, 48–56, 2 charts.

Several authors have reported that the chemical method of JONES (*Analyt. Chem.*, 1956, v. 28, 39) for estimating cycloserine shows that an apparent loss of the antibiotic occurs when it is incubated in the presence of serum. The authors of the present paper have shown that this apparent loss occurs immediately the cycloserine is added to serum but not when added to water, and they have also shown that the loss is not associated with a significant fall in antibacterial activity. The loss also occurs in deproteinized serum and, suspecting that it was due to amino acids, the authors have observed the effects of 16 of these acids; only methionine and cysteine were found to be active. As the fall is proportional to the concentration of cycloserine and is therefore not a constant quantity, the authors assumed that the amino acids combine with the sodium nitroprusside of the test reagents, thus preventing development of the maximum colour. Further experiments have confirmed this suggestion, and showed that precipitation of the amino acids by adding 10 volumes of acetone and the removal of the acetone by evaporation, allows the sodium nitroprusside method to be used without apparent loss of cycloserine. *S. R. M. Bushby*

VIALLIER, J. & CAYRÉ, R. M. Variabilité de la polyrésistance du bacille tuberculeux. I. Sensibilité au sel para-amino salicylique de l'isoniazide. [**Variability of Multiple Resistance of Tubercle Bacilli. I. Sensitivity to the PAS Salt of Isoniazid**] *C.R. Soc. Biol.* 1958, v. 152, No. 7, 1127–9.

Because of the heterogenicity of cultures of tubercle bacilli isolated from pathological specimens there is frequently an apparent resistance to 2 antituberculous drugs when tested separately but this resistance may disappear when the drugs are tested together, *e.g.* of 34 strains resistant to 10 μgm. streptomycin per ml. and 1 μgm. isoniazid per ml., 9 were sensitive when tested against the 2 drugs together.

Continuing these studies, the authors have determined the sensitivity of 236 strains to isoniazid and to its PAS salt (PI). 36 of these strains were resistant to 1 μgm. or more of the salt per ml. and 43 were resistant to 20 μgm. isoniazid per ml. The latter strains were also tested for PAS-sensitivity and the results were:—

		Strains sensitive to PI mgm. per ml.					
		less than 0·1	0·1–1	1–5	5–10	10–20	over 20
Sensitive to	1–5 μgm. PAS per ml.	8	14	6	2	3	1
,, ,,	5–10 ,, ,, ,, ,,	–	–	1	–	1	–
,, ,,	50–100 ,, ,, ,, ,,	–	–	1	–	–	–
Resistant to	100 ,, ,, ,, ,,	1	2	–	–	1	2

Therefore these isoniazid-PAS resistant strains were, in general, more sensitive to the salt of the 2 drugs than to the individual drugs and although the tuberculostatic activities of 7 sera and 5 urines of patients undergoing treatment with the salt were lower for a

strain resistant to isoniazid but sensitive to PAS, than for a strain sensitive to both drugs, the activities were nevertheless sufficient to be significant.

S. R. M. Bushby

VIALLIER, J. & CAYRÉ, R. M. Activité enzymatique et virulence de souches de *Mycobacterium tuberculosis* isoniazido-résistantes. [**Enzymatic Activity and Virulence of Isoniazid Resistant Strains of** *Mycobacterium tuberculosis*] *C.R. Soc. Biol.* 1958, v. 152, No. 7, 1156–8.

Of 135 cultures of tubercle bacilli grown from the sputum of 60 patients, 56 were resistant to over 20 μgm. isoniazid per ml. and were catalase negative. 65 strains were tested for isoniazid resistance, catalase activity and virulence to guineapigs; 19 were sensitive to 1–10 μgm. isoniazid, and 10 of them were catalase negative; 46 were resistant to 10 μgm. isoniazid and of these 34 were catalase negative.

The virulence of these strains was assessed by the extent of tuberculosis produced by a heavy inoculum (3–4 mgm. per kgm.) of each of the cultures injected into 2 guineapigs. Some relationship was found between virulence and the catalase activity; with some strains there were several exceptions in which medium or high virulence was shown by catalase-negative strains.

Somewhat better correlation was found between virulence and the sensitivity of the culture to hydrogen peroxide. Of 14 strains in which 80% or more of the bacilli were killed in 1 hour when immersed in 0·15% hydrogen peroxide, 3 were completely avirulent, 6 only slightly virulent and none was highly virulent, whereas of 11 strains of which less than 80% were killed, none was avirulent, only 2 were slightly virulent and 1 was highly virulent.

In general, the bacilli recovered from the guineapig lesion showed no significant change in catalase activity or isoniazid sensitivity. *S. R. M. Bushby*

TARSHIS, M. S. **Preliminary Observations on the Development of Atypical (Chromogenic) Variants of the H37Rv Strain of** *M. tuberculosis* **under the Influence of Streptomycin and Isoniazid** *in Vitro*. *Amer. Rev. Tuberculosis.* 1958, Dec., v. 78, No. 6, 921–6. [Refs. in footnotes.]

The object of these investigations was to determine whether exposure of H37Rv to streptomycin or isoniazid *in vitro* would produce atypical chromogenic variants.

In the first experiment, in which H37Rv was serially passaged at monthly intervals on Löwenstein-Jensen medium containing streptomycin, streptomycin variants capable of growing in 100 μgm. streptomycin per ml. were rapidly produced and after 14 months of sub-culturing on medium containing streptomycin, yellow colonies were growing; these colonies did not grow during sub-culturing on streptomycin-free medium. The colonies on further incubation developed into a variety of bizarre types and became finally orange. The organisms were Gram-positive but non-acid-fast, although some contained acid-fast granules. Similar changes occurred after 18 months of sub-culturing each fortnight in Tween-albumin liquid medium containing streptomycin and isoniazid separately.

These chromogenic variants were sub-cultured 24 times in 10 varieties of media, which included brain-heart infusion and thioglycollate broth, and from none were typical tubercle bacilli isolated. The variants were also injected into guineapigs and no typical tubercle bacilli were recovered from the tissues of the animals killed 2 and 4 weeks later.

The possibilities of these variants being contaminants were discounted, and attention is drawn to similar and related experiences of a number of other workers.

S. R. M. Bushby

O'GRADY, F. **Tuberculin Therapy of Mouse Thigh Tuberculosis.** *Brit. J. Exper. Path.* 1958, Dec., v. 39, No. 6, 582–8, 3 figs. [14 refs.]

SELBIE and O'GRADY [this *Bulletin*, 1955, v. 30, 441] showed that the intramuscular inoculation of tubercle bacilli into the thighs of mice produced a lesion of which the course could be followed by measurement, and the present author [*ibid.*, 1957, v. 32, 1102] has shown that the repeated injection of tuberculin into the other thigh produced a lasting reduction in the size of the tuberculous lesion. In the present paper, the extent to which the tuberculin injections controlled the lesion is reported.

The lesion, before entering into its healing stage, passed through 2 stages. There was a period of establishment lasting about 15 days and the inoculation of the tuberculin during this stage, at intervals of 3 and 4 days, produced a rapid fall in the size of the lesion amounting to about 50%, but with the cessation of treatment the lesions rapidly increased in size. With minimal doses of tubercle bacilli the lesions were either almost abolished or they appeared unaffected by the tuberculin.

The second stage lasted about 50 days, during which time the lesion increased in size; the tuberculin injections caused a temporary reduction in size, after which the lesion again increased in size to such an extent in some instances that it became larger than those of control animals. With lesions produced from minimal inocula the effects were very variable. In almost all instances the first injection of tuberculin produced an increase in the size of the lesion, followed by a marked decrease to the original level. In all the experiments there was an " escape " from the effects of the tuberculin after the 6th–10th injection.

The individual responses to the tuberculin consisted of 2 components; the first reached a maximum effect in 15 minutes and the second appeared after about 6 hours and reached a maximum in about 24 hours. In animals infected with 100 minimal doses the delayed reaction was not apparent with the first 2 injections.

The author considers that these complex responses may help to explain some of the differences of opinion regarding the efficacy of tuberculin therapy and he concludes that in view of the " escape " from these constant doses of tuberculin and the failure of response in the tuberculous lesions unless there is a delayed reaction, desensitization is unlikely to be the important factor in the value of tuberculin therapy. *S. R. M. Bushby*

KOGA, Y. **Tuberculosis and Stress.** *Jikeikai Med. J.* Minatoku. 1957, Sept., v. 4, No. 2, 171–90, 7 figs. [27 refs.]

Based on the observation that patients with various vague signs and symptoms diagnosed as neurosis may subsequently develop tuberculosis, the author suggests that early tuberculosis acts as the "stressor" in the SELYE conception of the stress syndrome. This contention is supported by the results of some experiments in guineapigs in which, 3–5 days after the intraperitoneal injection of H37Rv, the weight of the suprarenals was shown to be almost one-half that of normal glands, and there was histological evidence of atrophy of the cells and a temporary reduction in ketosteroid granules.

The author maintains that in the investigation of early tuberculosis, not only should the usual signs, such as tuberculin reaction, X-ray etc. be looked for but changes in the eosinophil and lymphocyte counts should be sought. *S. R. M. Bushby*

KELKAR, S. & RANADIVE, K. J. **Biological Factors in Transmission of Human Leprosy to Laboratory Animals. I.** *Indian J. Med. Sci.* 1958, Nov., v. 12, No. 11, 873–83, 6 figs. on pl. [20 refs.] **II.** *Ibid.*, 884–91, 6 figs. on 2 pls.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 543.]

KUSAKA, T. **Studies on the Metabolism of Murine Leprosy Bacilli. I. Stimulating Effect of Mitochondria Extract of Rat Liver on the Metabolism of Bacilli.** *Japanese J. Med. Sci. & Biol.* 1958, Aug., v. 11, No. 4, 277–85, 9 figs. **II. Substances, contained in Mitochondria Extract of Rat Liver, which stimulate the Metabolism of Bacilli and some Enzyme Systems in the Bacilli.** *Ibid.*, 287–93, 1 fig.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 544.]

MARWIN, R. M., with the technical assistance of J. A. VICK. **Use of Tellurite-Glycine Agar in the Detection and Isolation of Pathogenic Staphylococci.** *Amer. J. Clin. Path.* 1958, Nov., v. 30, No. 5, 470–72.

A modification of Zebovitz medium [this *Bulletin*, 1956, v. 31, 671] is recommended for the isolation of coagulase positive staphylococci from material from mixed clinical infections. This medium consists of 1·0% tryptone, 0·5% yeast extract, 0·5% mannitol, 0·5% K_2HPO_4, 0·5% lithium chloride, 1·0% glycine, 2% agar and 0·02% potassium tellurite. The author used a final *p*H of 6·2 instead of 7·2 which increased the specificity of the medium and he found it unnecessary to sterilize the potassium tellurite. This was obtained from the Baltimore Biological Laboratory and batches showed little variation in specificity. The medium keeps for a month in the refrigerator.

Coagulase positive staphylococci grow as black colonies in 24 hours. Test mixtures of these organisms with representative genera of organisms in specimens received for bacteriological examination proved that the medium was satisfactory, only a few coagulase negative staphylococci grew, and these were recognizable by their pale colour and small size. *M. Patricia Jevons*

BORMANN, F., with Helga PAULUS-BRACKER & Helga SCHNEIDER-SCHREIBER. Die Bedeutung der makroklimatischen Einflüsse für die Zusammensetzung der bakteriellen Assoziation der menschlichen Mund-, Rachen- und Nasenhöhle. [**Climate and the Bacterial Population of the Naso-Pharynx**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 3/4, 242–72, 5 figs. [24 refs.]

The author's conclusion is that the decrease in streptococcal infection during the present century, and the concurrent increase in staphylococcal, is attributable to the higher average temperature of the globe.

This thesis is supported, first, by records of a large number of cultures made on a very small number of persons over 2 years: streptococci were generally less common in the warmer season than in the cold, while staphylococci tended, somewhat irregularly, to be higher in the summer. Similarly staphylococci were found to overgrow streptococci and streptobacilli in the conjunctival sac of guineapigs kept under warm conditions, while the streptococci flourished in the cold.

Second, experiments with mixed cultures in broth showed that staphylococci tended to outgrow streptococci when the mixtures were held at 37°C., but the converse was true in cultures held at 10°C. Similar results were obtained with excised tonsils.

Third, cultures were posted to the author from healthy persons, and patients suffering from sore throat in various tropical regions. Staphylococci predominated over streptococci [but as the cultures were often in the post 5 days or more these results can have no significance]. *R. E. O. Williams*

GREENDYKE, R. M., CONSTANTINE, H. P., MAGRUDER, G. B., DEAN, D. C., GARDNER, J. H. & MORGAN, H. R. **Staphylococci on a Medical Ward, with special reference to Fecal Carriers.** *Amer. J. Clin. Path.* 1958, Oct., v. 30, No. 4, 318–22.

24% of 132 patients admitted to a medical ward in a New York hospital carried *Staphylococcus aureus* (not all strains so classed were coagulase-positive) and 78% of the strains were resistant to penicillin or to other antibiotics, or both. 19% of patients entering as non-carriers became carriers within their 10–14 days' stay, and many of the original carriers became carriers of penicillin-resistant strains. 15% of 136 patients yielded *Staph. aureus* from 1 or more rectal swabs.

Of 117 strains submitted to phage typing 101 could be typed and 46 fell into 1 or other of 3 types—1 of which (44A/81/42B with 52 and 52A [= 80 or 80/81]) is a well-known epidemic type. There was, however, no evidence of an undue prevalence of sepsis in the hospital at the time. *R. E. O. Williams*

BURKINSHAW, J., HAMER, J. & SWIER, J. **Staphylococcal Nasal Carrier Rates in a Maternity Hospital.** *New Zealand Med. J.* 1958, Aug., v. 57, No. 320, 366–9.

The carrier rate of coagulase positive staphylococci in the noses of 113 mothers admitted to a 44-bed maternity hospital during a period free from sepsis rose only from 30%–36% by the tenth day. The nasal carrier rate in babies rose from 19% on the 4th day to 34% on the 10th day and the carrier rate in nurses was 43%.

55% of all strains, which belonged to a variety of phage types, were penicillin resistant. The pattern of antibiotic resistance of strains isolated from babies was similar to that of the nurses rather than that of the mothers [this *Bulletin*, 1955, v. 30, 814; 1956, v. 31, 334].

The authors recommended regular nasal swabbing of nursery staff to detect "dangerous" types.

M. Patricia Jevons

TAPLIN, Jennifer & GOLDSWORTHY, N. E. **A Study of 225 Strains of *Staphylococcus* isolated from the Mouth.** *Australian J. Exper. Biol. & Med. Sci.* 1958, Aug., v. 36, Pt. 4, 289–304. [17 refs.]

225 strains of staphylococci isolated from the saliva of 130 healthy children were submitted to a large number of physiological tests and were then classified either according to BERGEY's manual [6th edition, 1948, since when the 1957 edition has appeared, modifying this classification], or to SHAW, STITT and COWAN [this *Bulletin*, 1952, v. 27, 484]. 79 of these strains produced coagulase; 15 of the coagulase-positive and 17 of 146 coagulase-negative strains were penicillin resistant. The correlations between the 2 classifications, and the number of atypical strains for each, are discussed.

R. E. O. Williams

KNIGHT, V., WHITE, A. C. & MARTIN, Margaret P. **The Effect of Antimicrobial Drugs on the Staphylococcal Flora of Hospital Patients.** *Ann. Intern. Med.* 1958, Sept., v. 49, No. 3, 536–43, 4 figs.

The authors first recall the published experience of Knight and his colleagues [this *Bulletin*, 1955, v. 30, 70; 1957, v. 32, 375], namely that hospital patients treated with tetracyclines or to a less extent penicillin rapidly become nasal carriers of drug-resistant hospital staphylococci. The drugs are thought to cause this effect by eliminating drug-sensitive strains from the nose and allowing its recolonization with resistant strains from this environment. In the authors' experience colonization of non-carriers by the hospital strains appears to have been unusual.

In their studies in 1957–8, in Nashville, Tenn., 55% of the coagulase-positive strains belonged to phage group I, predominantly the type now known as 80 or 80/81, and were mostly highly susceptible to penicillin and tetracyclines; this contrasts with earlier experience, in which most of the strains were of group III and were resistant.

The 1957–8 studies were made in a mental hospital where only occasional doses of antibiotics had been given; the earlier studies were made in general hospitals. The authors suggest that control of resistance could be approached by periodically withholding certain drugs from use in hospitals. *R. E. O. Williams*

ANDRIEU, G., MONNIER, J. & BOURSE, R. Corrélations entre les sensibilités à quatorze antibiotiques d'un lot de staphylocoques pathogènes d'origine humaine. [**Correlations Between the Sensitivity to 14 Antibiotics of Pathogenic Staphylococci of Human Origin**] *C.R. Soc. Biol.* 1958, v. 152, No. 5, 870–74.

These authors from Toulouse have determined the minimum inhibitory concentrations of 14 antibiotics for 324 strains of *Staphylococcus aureus*, and calculated coefficients of correlation between the results: a high coefficient is an expression of regularity of cross-resistance. High coefficients were obtained for all pairs of the 3 tetracyclines, neomycin and framycetin, and erythromycin and oleandomycin (but not carbomycin or spiramycin). An apparently significant but lower figure for penicillin and streptomycin is regarded as a "false correlation", due to the fact that so many strains are now resistant to both the antibiotics which have been longest in use. *L. P. Garrod*

ROBINSON, J., THATCHER, F. S. & GAGNON, Jeannine. **Studies with Staphylococcal Toxins. IV. The Purification and Metallic Requirements of Specific Hemolysins.** *Canadian J. Microbiol.* Ottawa. 1958, Aug., v. 4, No. 4, 345–61, 8 figs. [36 refs.]

Staphylococci were grown in a semisolid medium in an atmosphere of 10% CO_2 and 90% O_2; the bacteria and agar were separated by spinning and the haemolysin in the supernatant was purified by precipitation with ethanol at −20°C. and ammonium sulphate, and with a calcium phosphate gel as adsorbent. This was followed by electrophoresis on a starch column. Haemolysin activity was measured as the amount of haemin liberated from washed red cells.

Most of the experiments were made with a staphylococcus whose crude filtrate produced "α" and "β" toxin and enterotoxin. Although 2 haemolysins with differing biological and electrophoretic characters were isolated they could not be equated with these classical toxins, and serologically they were indistinguishable. Some effects of metallic ions on the haemolytic activity of the preparations are reported; ethylene diamine tetra-acetic acid was inhibitory, and this effect could be reversed by manganese, cobalt, nickel, iron and magnesium, but not by calcium or zinc.

The authors stress their view that the classical separation of α and β haemolysins may be an artefact attributable to the impurity of the preparations.

[For previous parts of this series, see this *Bulletin*, 1956, v. 31, 80.] *R. E. O. Williams*

TONELLI, E. & MARINELLI, M. Sull'attività fosfatasica dello stafilococco. [**Phosphatase Activity of Staphylococci**] *Nuovi Ann. d'Igiene e Microbiol.* 1958, Sept.–Oct., v. 9, No. 5, 461–7. [14 refs.]

The English summary appended to the paper is as follows:—

"The phosphatase activity of 31 strains of *Staphylococcus* have been studied at various pH, after 12 hours and some culture days. Disodic phenylphosphate has been employed as substratum. The obtained results may be summarized as follows:

"1) 12 strains did not show any phosphatase activity at all.

"2) The enzymatic action of all the phosphatase positive strains was observed from pH 4.2 to pH 9.3: its maximum at pH 7.6; however, the greatest part of the strains develops an hydrolytic action of the same intensity also at pH 7 or pH 8.

"3) In the phosphatase positive broth-cultures the greatest values of the enzyme have been observed after 2 culture days; in older cultures (5–8 days) the clear decreasing of the alkaline phosphatase has been ascertained."

JOHANOVSKÝ, J. **Role of Hypersensitivity in Experimental Staphylococcal Infection.** [Correspondence.] *Nature.* 1958, Nov. 22, v. 182, 1454, 1 fig.

A state of hypersensitivity was induced in rabbits by repeated injections of small numbers of staphylococci. Spleen cells or peritoneal exudate (induced by saline injection) from these animals were injected intraperitoneally into normal rabbits, which were, next day, tested for skin sensitivity to toxoid and vaccine, and then challenged intravenously with 2×10^6 virulent staphylococci.

The transfer of cells led to delayed skin hypersensitivity [this *Bulletin*, 1956, v. 31, 389] and increased susceptibility to infection: 21–26% of various control animals (55 in all) died, compared with 71% of the animals receiving cells and 81% of the hypersensitive animals themselves.

[See also *ibid.*, 1956, v. 31, 1161].

R. E. O. Williams

RICHMOND, M. H. **Lytic Enzymes of *Staphylococcus aureus* 524.** *Biochim. et Biophys. Acta.* 1959, Feb., v. 31, No. 2, 564–5, 2 figs.

TOWERS, A. G. & GLADSTONE, G. P. **Two Serological Tests for Staphylococcal Infection.** *Lancet.* 1958, Dec. 6, 1192–5, 8 figs. [18 refs.]

A number of surveys have shown the normal serum titre of staphylococcal antihaemolysin to be 2 units per ml. or less. However, many cases, even of osteomyelitis have titres within the same range; the antileucocidin titre was therefore examined as an alternative.

The antihaemolysin titre was taken as the reciprocal of the dilution allowing 50% haemolysis of red cells in the presence of 1 haemolytic unit of a standard toxin. The antileucocidin titre was derived from the highest serum dilution allowing the production of morphological changes in the leucocytes by a standard leucocidin preparation [this *Bulletin*, 1957, v. 32, 900]. The upper limit for normal was taken as 10 units per ml.

Sera were examined from 83 patients with staphylococcal infection (69 osteomyelitis) and 73 with non-staphylococcal disease. On admission to hospital all the patients in the latter group had antihaemolysin titres below 2, but 17% had antileucocidin titres above 10; only 33% of sera from patients with staphylococcal disease had raised antihaemolysin titres at this stage compared with 82% for antileucocidin. Studies of the titres during the progress of the disease suggested that though both antibodies showed distinct fluctuations, the antileucocidin shows the greater variation in acute osteomyelitis, and the antihaemolysin persists at a higher level in long-standing disease.

R. E. O. Williams

BELL, J. F., OWEN, Cora R. & JELLISON, W. L. **Group A Streptococcus Infections in Wild Rodents.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 196–203, 6 figs.

During an "eruption" of several kinds of rodents in the N.W. United States in 1957 up to 19% of the animals were found to have a disease, not necessarily fatal, characterized chiefly by swollen limbs and sometimes by internal abscesses. This appeared to be due to infection with group A haemolytic streptococci, which typically grew much better anaerobically at room temperature than aerobically or at 37°C. The disease could be reproduced artificially by injection, especially into the foot-pad.

R. E. O. Williams

KRAUSE, R. M. **Studies on the Bacteriophages of Hemolytic Streptococci. II. Antigens released from the Streptococcal Cell Wall by a Phage-Associated Lysin.** *J. Exper. Med.* 1958, Dec. 1, v. 108, No. 6, 803–21, 11 figs. [35 refs.]

Phage lysates active on group C streptococci contain a substance which lyses groups A and C streptococci [this *Bulletin*, 1957, v. 32, 1093; 1958, v. 33, 77]. This lysin was separated from phage by precipitation with ammonium sulphate and differential centrifugation. The lysin was shown to release almost all the group A and C carbohydrates from isolated cell walls, and thus provided a method of purifying the antigens. Group C antigen obtained this way behaved the same way as C antigen released by the action of an enzyme from *Streptomyces albus*, when subjected to electrophoresis, ultracentrifugation, precipitation with antiserum and chemical analysis. Antigen released by both enzymes inactivated group C phage specifically.

M protein was also found to be released by the action of the phage-associated lysin. It was homogeneous on electrophoresis, but appeared to contain some protein other than M and some group-specific carbohydrate bound to protein.

Janice Taverne

HOLMES, Margaret C. **Type Specific Antibodies to *Streptococcus pyogenes*.** *Australian J. Exper. Biol. & Med. Sci.* 1958, Aug., v. 36, Pt. 4, 395–403.

Sheep red cells were treated with 1/50,000 tannic acid and sensitized with M antigen, which had been

prepared from a Lancefield extract of whole streptococci by precipitation with 2 volumes of alcohol. When cells sensitized with dilutions of antigen were tested for haemagglutination with type-specific rabbit antisera, numerous cross-reactions were observed, even though these sera showed no cross-reactions in M precipitin tests. After various tests it was found that the cross-reactions could be removed by absorption with a suspension of type 14 and of type 31 streptococci.

52 sera, mostly collected from children undergoing tonsillectomy, were absorbed with type 14 and 31 streptococci, and with sheep red cells, and were then tested for haemagglutination against 17 red cell suspensions sensitized with different type antigens. 31 reacted with one or other cell suspension, 7 of them reacting with two, 5 with three and 3 with four antigens. The commonest types to react were 1, 6 and 12, which are also the commonest types recovered from children in the locality. Multiple reactions appeared to be due to the presence of antibodies to more than 1 type. [No tests are reported on convalescent sera from patients known to have been infected with particular streptococcal types.]

R. E. O. Williams

JOHNSON, B. H. & FURRER, W. **Hyaluronic Acid: a Required Component of Beta Hemolytic Streptococci for infecting Mice by Aerosol.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 135–41, 2 figs. [10 refs.]

Earlier experiments by COBURN, FRANK and NOLAN [this *Bulletin*, 1957, v. 32, 996] in which mice were infected with haemolytic streptococci by exposure to an aerosol of the organisms gave some indication that the strains that were best able to infect mice had mucoid colonies. Further similar experiments were therefore made to test the relation between the hyaluronic acid production of streptococci and their ability to infect. None of 4 strains giving no hyaluronic acid reaction at a 1 : 80 dilution of culture fluid was able to infect normal mice by the respiratory route; while 7 strains giving a 1+ or 2+ reaction at this dilution all killed 50% or more of the mice (usually 12 in number) tested. The infectivity of 1 strain could not be reduced by passage in hyaluronidase broth nor could that of another be enhanced by adding hyaluronic acid to the growth medium.

R. E. O. Williams

SYRUCEK, L. & BRUCKOVÁ, M. **Notes on the Determination of Sulphonamide Resistance in Beta Haemolytic Streptococci** *in vitro*. *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 2, 155–71, 9 figs. (4 on pl.) [44 refs.]

These authors from Prague reported in 1952 that 77% of 368 strains of haemolytic streptococci were resistant to sulphathiazole. That so many strains of Czechoslovakian streptococci should be sulphonamide-resistant evidently caused surprise when reported at a symposium on the Prevention of Rheumatism in Paris in 1956, and the present work was undertaken to convince the sceptics of its truth. Unfortunately the findings may not have this effect: they are very difficult to interpret in any sense. 3 different media were used in the main tests, in 2 of which 86% and 83% of strains were found to be resistant to sulphathiazole whereas in the other, a semi-synthetic medium which the authors consider unsuitable, none were. It was shown that the peptone used did not contain sulphonamide antagonists: it was also shown that if horse blood were substituted for the sheep blood used, all resistant strains became sensitive: the authors do not accept the usual belief that lysed horse blood merely neutralizes sulphonamide antagonists, but state that it contains a factor "which makes it possible for sulphonamides to take effect *in vitro* even on strains demonstrated as being resistant".

That some of the allegedly resistant strains were actually resistant is claimed to have been shown by therapeutic tests in mice: in those infected with 5 resistant strains the mean mortalities were about 50% in both treated and control mice, whereas in those infected with 4 sensitive strains the mortality was 19% in the treated and 59% in the controls. [These results would have been more convincing if an inoculum had been used producing 100% mortality in controls.]

L. P. Garrod

SULITZEANU, D. **Relationship of Agar Diffusion Patterns to Agglutinating and Protective Properties of *Brucella suis* Antisera.** *Brit. J. Exper. Path.* 1958, Aug., v. 39, No. 4, 367–75, 5 figs. on 2 pls.

For this work a considerable battery of antisera to *Br. suis* cultures and various fractions derived from them has been prepared. *Br. suis* strains have been employed in this investigation because with them sera rich in precipitins are more easily obtained and hence give more sharply distinguished lines in Ouchterlony plates. As many as 7 separate lines may be obtained in such plates where the reference serum used was put up with the appropriate culture. 5 of these were obtained with regularity and by means of absorption with different bacterial preparations, extracts and residues, one or more of these could be eliminated.

From such studies the following conclusion is reached: the antibodies involved in agglutination and in protection tests are mainly independent of those responsible for the lines of precipitation, *i.e.* the antigens which stimulate production of protective antibodies and of agglutinins are insoluble and carried by the cell framework left after elaborate sonic disintegration. It is also noted that the rise in agglutinins occurs early and that in precipitins later and the suggestion is made that the continued rise of agglutinin which appears to correspond to protective antibody suffers from competition with the soluble antigen components.

J. W. McLeod

PITTMAN, Margaret. **Effect of *Haemophilus pertussis* on Immunological and Physiological Reactions.** *Federation Proc.* Wash. 1957, Sept., v. 16, No. 3, 867–72, 1 fig. [63 refs.]

The author gives a comprehensive review of the literature on some of the outstanding physiological and

immunological reactions induced by *Haemophilus pertussis*. The increased susceptibility of mice to a number of agents conferred by *H. pertussis* has been related to their non-specific resistance which the author says may be 2 phases of one reaction induced by pertussis organisms. The nature of these reactions has been discussed. *F. T. Perkins*

KOROBKOVA, E. I. **Concerning the Methods of increasing the Immunogenic Properties of Various Strains of Plague Vaccines and their Stabilization.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 7/8, 985–9. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 532.]

KLEINMAIER, H., SCHREINER, E. & GRAEFF, H. Untersuchungen über die serodiagnostischen Differenzierungsmöglichkeiten mit thermolabilen Antigenen von *Pseudomonas aeruginosa*. [**Serological Differentiation of *Pseudomonas pyocyanea* with the help of Thermolabile Antigens**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, June, v. 115, No. 6, 492–508. [13 refs.]

DE BRUIJN, J. H. **Investigations into the Antigenic Structure of the Reiter Strain of *Treponema pallidum*. I. The Presence of the "Ubiquitous Lipid" in the Protein Fraction.** *Antonie van Leeuwenhoek; J. Microbiol. & Serol.* 1958, v. 24, Nos. 3/4, 253–6.

A protein fraction of the Reiter spirochaete provides a suitable antigen for serum tests for syphilis [this *Bulletin*, 1958, v. 33, 33]; it also seems likely that syphilitic serum contains at least 3 separate antibodies. This author therefore investigated the presence of a "minor" component of the protein fraction; for this purpose the protein fraction was treated with absolute ethanol, the supernatant evaporated and the residue dissolved in distilled water or ethanol.

Syphilitic serum was absorbed with cardiolipin antigen [for details the original should be consulted] and the original and absorbed sera titrated with protein antigen; little difference was noted.

When the alcohol soluble fraction of protein antigen was used as antigen all results were negative with the cardiolipin absorbed syphilitic serum though with the original serum positive results were obtained up to a dilution of antigen 1/10. Thus the major component of protein antigen was precipitated by ethanol but the minor component remained; this latter is phosphatidic in nature.

It is concluded that protein antigen contains "ubiquitous lipid", that the minor component appears to be related to cardiolipin antigen and that biologic false positive results are not likely to occur provided the protein antigen is used in a sufficiently high dilution. *T. E. Osmond*

AHRENS, C. B. F. W. & MUSCHNER, K. Zum gegenwärtigen Stand der Spirochätenätiologie der Multiplen Sklerose. Ein Borrelienbefund bei einem MS-Fall. [**Present Status of the Spirochetal Etiology of Multiple Sclerosis. Borrelia Findings in a Case of Multiple Sclerosis**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 5/6, 462–71, 3 figs. [33 refs.]

The authors used the SIMONS technique [*Trop. Dis. Bull.*, 1955, v. 52, 1089] to investigate brain lesions from a case of multiple sclerosis. This technique had been successfully employed in investigating the brains of mice artifically infected with *Borrelia*. The present report concerns investigations on the brain removed from a patient who died from multiple sclerosis 30 hours after death and macerated in 7% alcohol. Examination of material from the older lesions failed to show any *Borrelia* but 2 were found in more recent lesions. Morphologically they were 6 to 11μ long with 3 to 5 coils and appeared more frail and delicate than organisms found in the brain of mice infected with *Borrelia* [*Spirochaeta*] *duttoni*. *P. A. Clearkin*

ROACH, L. L., Jr., ROSENBERG, S. & ICHELSON, Rose R. **Immunological Considerations of an Antigenic Fraction from Cultures of Spirochetes isolated from Cerebrospinal Fluid of Multiple Sclerosis Cases: Preliminary Report.** *Amer. J. Med. Sci.* 1959, Jan., v. 237, No. 1, 8–11.

The English summary appended to the paper is as follows:—

"1. An antigen was prepared from spirochetes cultured from spinal fluids of multiple sclerosis cases and was used in a complement fixation technique to diagnose multiple sclerosis in sera sent to this laboratory without diagnostic data.

"2. The medium used for culturing the spirochetes was that devised by Ichelson. The method of preparing the antigen is described above. The complement fixation test used was the Kolmer one-fifth volume test as modified by Portnoy and Magnuson.

"3. The results indicate that fixation occurred in 77% of all cases with histories of multiple sclerosis and 26% of cases with normal or other pathological findings.

"4. Case histories as to the duration and intensity of the disease were not supplied. Further studies are in progress."

SORU, Eugenia, ISTRATI, Maria, POENARU, Elena & STENBERG, M Étude chimique comparative de la toxine et de l'anatoxine tétanique. [**A Comparative Chemical Study of Tetanus Toxin and Toxoid**] *Arch. Roumaines Path. Expèr. et Microbiol* 1958, June, v. 17, No. 2, 283–8. [11 refs.]

The English summary appended to the paper is as follows:—

"The amino acid contents and N-terminal groups

were determined in tetanus toxin and toxoid purified with hexametaphosphoric acid.

"The homogeneity of the preparations used was checked electrophoretically. The protein nature of the preparations was confirmed by adsorption spectra in ultraviolet light ($\lambda = 274$).

"Amino-acids were determined qualitatively and quantitatively by partition chromatography on filter paper.

"N-terminal amino-acids were determined by dinitrophenylation with dinitrofluorobenzene and separation by partition chromatography on filter paper. As a consequence of detoxification of tetanus toxin by means of formaldehyde and toxoid formation, the following changes were noticed to occur:

"1. Disappearance of tyrosine.

"2. A decrease in the concentration of certain amino-acids; cysteine, histidine, arginine, aspartic acid, proline, methionine, phenylalanine, lysine, tryptophan.

"3. The disappearance to a large extent of aspartic acid as an N-terminal group."

GARROD, L. P. **The Chemoprophylaxis of Gas Gangrene.** *J. Roy. Army Med. Corps.* 1958, Oct., v. 104, No. 4, 209–15. [15 refs.]

This paper presents a brief review of recent work on the sensitivity of gas-gangrene clostridia to antibiotics *in vitro* and in infections of laboratory animals, and it reports the author's own investigations on the *in vitro* sensitivity of 10 species of clostridia to 16 antibiotics. The minimal inhibitory concentrations of penicillin, streptomycin, chloramphenicol, chlortetracycline, oxytetracycline, tetracycline, erythromycin, spiramycin, oleandomycin, carbomycin, E 129 [this *Bulletin*, 1956, v. 31, 1034], novobiocin, vancomycin, bacitracin, polymyxin, and neomycin were determined for 5 strains each of *Clostridium welchii* and *Cl. tetani*, 3 each of *Cl. septicum*, *Cl. oedematiens*, *Cl. histolyticum*, and *Cl. sporogenes*, 2 each of *Cl. bifermentans*, *Cl. tetanomorphum*, and *Cl. tertium*, and 1 strain of *Cl. sphenoides*. Tests were performed by inoculating drops of broth cultures on to the surface of a series of lysed-blood-agar plates containing 2-fold dilutions of antibiotic. Plates were read for growth after 24 hours' anaerobic incubation.

All the organisms were highly resistant to streptomycin, neomycin and polymyxin and only slightly less resistant to novobiocin and bacitracin. Erythromycin, spiramycin, oleandomycin, carbomycin, chloramphenicol and vancomycin were all less active than penicillin and the tetracyclines, which were the most effective antibiotics tested. E 129 came closest to penicillin and the tetracyclines in activity. Chlortetracycline was more active than the other 2 tetracyclines. Penicillin and a tetracycline when tested in combination showed an additive effect.

The author considers that although chlortetracycline is the most active antibiotic against clostridia, penicillin would be the antibiotic of choice under battle conditions because it may be readily administered intramuscularly. *I. B. R. Duncan*

BRADLEY, D. E. & FRANKLIN, J. G. **Electron Microscope Survey of the Surface Configuration of Spores of the Genus** *Bacillus*. *J. Bacteriology*. 1958, Dec., v. 76, No. 6, 618–30, 76 figs. [11 refs.]

HARRIS-SMITH, Patricia W., SMITH, H. & KEPPIE, J. **Production** *in vitro* **of the Toxin of** *Bacillus Anthracis* **previously recognized** *in vivo*. *J. General Microbiol.* 1958, Aug., v. 19, No. 1, 91–103. [11 refs.]

The work of SMITH, KEPPIE and STANLEY [this *Bulletin*, 1956, v. 31, 585] on the production of toxin by anthrax B in the circulation of the experimental animal has been followed up and the authors have demonstrated production of a similar toxin although a slightly weaker one *in vitro*. The medium used is guineapig serum 90% and tryptic meat digest 10% and the essential points appear to be the presence of a considerable amount of material of high molecular weight in the medium and the separation of toxin at an early stage in cultures—3 to 4 hours. If the culture grows for longer and the bacterial population becomes more dense, then the bacteria themselves destroy the toxin.

No clear explanation of this destruction is offered.

[It is noteworthy that in respect of requirement of nutrients of high molecular weight and optimal yield of toxin in the early hours of culture, there is an analogy with production of S haemolysin and lethal toxin (rabbit) by the streptococcus.] *J. W. McLeod*

BARBER, Cella, ZILIŞTEANU, Eugenia & NAFTA, I. Une nouvelle méthode de séparation de l'acide polyglutamique du *Bacillus anthracis*. [**A New Method for the Isolation of Polyglutamic Acid from** *B. anthracis*] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, June, v. 17, No. 2, 279–82, 1 fig.

The English summary appended to the paper is as follows:—

"By means of a simple method affording a very good yield the specific polypeptide of a bacillus anthracis strain incapsulated in ordinary culture media (48 hours) was isolated in a highly polymerized state.

"The method implies treatment of the germs with 90 per cent. phenol (which is discarded) and their subsequent suspending in physiologic saline into which the polymer passes readily."

CARACÒ, A. & GRAVINA, E. Ossidazione degli aminoacidi da parte del *Bacillus anthracis*. [**Oxidation of Amino Acids by** *Bacillus Anthracis*] *Riv. Istituto Sieroterap. Ital.* 1958, Nov.–Dec., v. 33, No. 6, 409–13. English summary (6 lines).

NOMURA, M. & YOSHIKAWA, H. **Stimulation of Amylase Formation by a Ribonucleic Acid Preparation from** *Bacillus subtilis*. *Biochim. et Biophys. Acta.* 1959, Jan., v. 31, No. 1, 125–34, 7 figs. [22 refs.]

STUY, J. H. **Nucleic Acid Synthesis in Ultraviolet-Irradiated** *Bacillus cereus*. *J. Bacteriology*. 1958, Dec., v. 76, No. 6, 668–9.

FUNGI

BLYTH, W. **The Influence of Antibiotics on Experimental Moniliasis. I. Penicillin, Streptomycin, Chloramphenicol and Viomycin.** *Mycopathologia*. The Hague. 1958, Dec. 30, v. 10, No. 2, 91–112, 12 figs. [36 refs.]

In these experiments mice received intraperitoneal injections of antibiotics, and were inoculated with *Candida albicans* by the same route afterwards. 2 strains of this organism were used, and an inoculum of 2 different magnitudes of each, and 15 different antibiotic treatments were given. According to Tables II and III only 99 mice were used in experiments providing for all these variables, many of the treatments being given to only 1 mouse in each group. This variety was attained by giving either 1 or 2 doses of streptomycin, penicillin, chloramphenicol or viomycin before inoculation, with or without a single dose after it, or giving 1 dose each of all 4 antibiotics before it, the interval between all injections, whether of antibiotics or culture, being 24 hours. The main conclusion reached is that pre-treatment with either streptomycin or all 4 antibiotics reduced resistance, the infection produced being more acute or extensive than in untreated controls. On the other hand, penicillin, chloramphenicol and viomycin are considered to have afforded "protection". [There is little reason why they should, *C. albicans* being highly resistant to all of them. These experiments need repetition, if they are worth doing at all, in simplified form with adequate numbers of animals.] The author speculates somewhat diffusely on the nature of this "enhancement" by streptomycin, and describes the tissue changes observed: there are illustrations of suppurative lesions in 5 hearts and 7 kidneys. *L. P. Garrod*

DOBEK, Maria. Action de l'isoniazide sur *Nocardia asteroides in vitro* et *in vivo*. [**Action of Isoniazid on** *Nocardia asteroides in vitro* **and** *in vivo*] *Ann. Inst. Pasteur*. 1959, Jan., v. 96, No. 1, 116–19. [10 refs.]

The English summary appended to the paper is as follows:—

"The strains studied are completely inhibited by high concentrations of isoniazid (2,500 to 5,000 μg/ml.). However, one strain, different from the type species, is completely inhibited by 156 μg/ml. The partially inhibiting concentrations vary according to the strains between 40 and 2,500 μg/ml.

"Isoniazid does not influence the course of experimental nocardiosis, nor *Actinomyces* present in the organs. There is a relationship between the pathogenicity of the strains and their sensitivity to isoniazid.

"All the strains studied are catalase-positive. The oldest cultures are the less active. The different culture media have no influence.

"No loss of catalase activity has been noticed in strains grown in the presence of isoniazid. *N. asteroides* has then the same comportment as saprophytic or atypic *Mycobacteria*."

RICKETTSIAE

MITEREVA, V. G. **Experimental Use of Fluorescence Microscopy in the Study of Rickettsia.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 5, 674–7. [Translated from Russian.]

PSHENICHNOV, A. V., SHEVELEVA, O. N. & NOSKOVA, E. G. **Variability of** *Rickettsia prowazeki* **and Prospects of obtaining Live Typhus Vaccine.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 7/8, 935–8. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 522.]

BACTERIOPHAGES

SYMONDS, N. & MCCLOY, Elinor W. **The Irradiation of Phage-Infected Bacteria: its bearing on the Relationship between Functional and Genetic Radiation Damage.** *Virology*. New York. 1958, Dec., v. 6, No. 3, 649–68, 5 figs. [25 refs.]

Escherichia coli cells were singly infected with T2 or T4 and then subjected to different kinds of radiation at intervals during the first 7 minutes of the latent period of the phage. The resistance of T2 phage to soft X-rays and to inactivation by the decay of incorporated ^{32}P atoms, and the resistance of T4 phage to irradiation with UV light, stayed constant for the first 5 minutes and then increased sharply. The resistance of T2 to UV rays did not stay constant however, but increased slowly for 5 minutes, when it also rose sharply. Some of the inactivation of T2 by UV light could be reversed by photoreactivation, but the amount of reactivation was found to decrease during the first 5 minutes of the latent period.

It is likely that after 5 minutes of infection the greater resistance of phage to radiation arises because genetic information previously carried only by parental phage DNA is passed to some more resistant form, *e.g.*, to a nucleoprotein. The authors suggest that during these first 5 minutes phage can be inactivated either by genetic damage, preventing replication of DNA, or by "functional" damage, in which an essential biochemical step in early phage synthesis is blocked. A given dose of irradiation at any time in the first 5 minutes (when only 1 copy of genetic information exists) must cause the same amount of genetic damage. For this and other

reasons the authors conclude that UV-inactivation of T2 which can be reversed by photoreactivation results only from functional damage, whereas inactivation by ionizing radiations and the UV-inactivation which cannot be reversed by photoreactivation may result from both functional and genetic damage. *Janice Taverne*

LEVINE, L., BARLOW, J. L. & VAN VUNAKIS, Helen. **An Internal Protein in T2 and T4 Bacteriophages.** *Virology.* New York. 1958, Dec., v. 6, No. 3, 702–17, 6 figs. [36 refs.]

Antiserum prepared against broken up T2 phage particles and absorbed with whole phage or with ghosts was still found to contain a complement-fixing antibody against the disrupted phage. It appeared that an internal antigen, not normally exposed in the protein coat, had been released from the phage. The same amount of this antigen was released whether phage was broken up by urea, pyrophosphate, alkali, heat, freezing and thawing, osmotic shock or sonic oscillation. 90% of its immunological activity was destroyed by proteolytic enzymes and 10% by DNase. It was purified and found to comprise 4–6% of the total phage protein N. It did not cross-react with antisera made against disrupted T4, although the external antigens of T2 and T4 cross-react. When T2 ejected its DNA after adsorption to bacterial cell walls, it also ejected the internal protein.

Other workers have shown that a small amount of protein accompanies T2 DNA into the bacterial cell [this *Bulletin,* 1958, v. 33, 397]. It is also known that some protein synthesis occurs in the infected cell before DNA replication begins. Some of the internal protein described here was shown to be synthesized before phage DNA or ghost protein.

The authors speculate that their internal protein could form a backbone for DNA or even carry genetic information, functions which it has been suggested protein might fulfil. *Janice Taverne*

THOMAS, C. A., Jr. **The Release and Stability of the Large Subunit of DNA from T_2 and T_4 Bacteriophage.** *J. General Physiol.* 1959, Jan. 20, v. 42, No. 3, 503–23, 6 figs. [30 refs.]

"T_2 and T_4 bacteriophage have been exposed to various treatments which are known to release the encapsulated DNA. The unseparated reaction products have been examined by autoradiography. The results indicate the presence of one large subunit of DNA (molecular weight 45×10^6) for each former phage particle. Some smaller subunits of molecular weight 12×10^6 have been observed.

"The large subunit is sensitive to very small amounts of DNAase, and is resistant to mixed proteases and cannot be dispersed by banding in cesium chloride density gradients.

"The sensitivity to fragmentation by P^{32} decay and the increase in this sensitivity following heat treatment are best explained by assuming that the large subunit is a duplex of polynucleotide strands over most of its length.

"The presence of hypothetical non-DNA interconnections is considered."

VIRUSES

In this section the abstracts are arranged as far as possible in the following order: General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; Others.

PULVERTAFT, R. J. V., DAVIES, Joan R., WEISS, L. & WILKINSON, J. H. **Studies on Tissue Cultures of Human Pathological Thyroids.** *J. Path. & Bact.* 1959, Jan., v. 77, No. 1, 19–32, 9 figs. on 4 pls. [36 refs.]

The authors point out that thyroid tissue is frequently removed in a general hospital, and have demonstrated that monolayer cultures of cells may be readily obtained from it by standard methods of trypsinization [see DULBECCO and VOGT, this *Bulletin,* 1954, v. 29, 887]. The cells settle on to the glass and spread out to form a sheet more quickly than cells from other sources (*e.g.,* kidney), confluent primary cultures being usual after 48 hours. The cells are usually spindle-shaped and survive as a healthy sheet for 14 days but thereafter tend to disintegrate and fall off the glass. Between 3 and 6 weeks several foci of smaller polyhedral refractile cells are observed. These cells grow out to cover the culture vessel and may be subcultivated.

The authors now maintain 4 separate lines of these "transformed" cells. The cells grow well in Hanks saline with yeast extract and lactalbumin hydrolysate and 10% serum (usually human, but rabbit or horse is said to be satisfactory). Transformed cells resemble HeLa cells and the cells derived in a similar manner by WESTWOOD *et al.* [*ibid.,* 1957, v. 32, 815]. Cells derived from toxic or non-toxic goitre and from carcinoma of the thyroid (2 samples) show morphologically similar primary and "transformed" cells. Cells in primary culture differ from the transformed cells in other respects besides appearance. Whereas the primary cells still synthesize organic iodine compounds the transformed cells do not. There is also a change in viral susceptibility, the primary cells being susceptible to Coxsackie A9, ECHO 6 and 9 (like primary monkey kidney cells) and not to Coxsackie A13 whereas the susceptibility of the transformed cells (like that of HeLa cells) is exactly opposite. Both types of cell are sensitive to poliovirus, Coxsackie A2, B1 and adenovirus types 1–11. The transformed thyroid cell lines were equally sensitive to poliovirus as other transformed cell lines. The fresh cells appeared to produce poliovirus in high titre (10^5 per ml.) but only showed cytopathic effects with low dilutions (1/20). These cells were very sensitive to small amounts of poliovirus but subculture into cells showing a cytopathic effect is necessary to demonstrate the fact.

The value of these easily obtainable cells in studies of cell transformation, thyroid function (the effect of

serum from cases of Hashimoto's disease or the role of colloid in the synthesis of thyroid hormones, for example) and virology are stressed. *A. J. Beale*

TAVERNE, Janice, MARSHALL, J. H. & FULTON, F. **The Purification and Concentration of Viruses and Virus Soluble Antigens on Calcium Phosphate.** *J. General Microbiol.* 1958, Dec., v. 19, No. 3, 451–61, 4 figs. [19 refs.]

Chromatography in calcium phosphate columns was used for the concentration and purification of several animal viruses. Crude preparations of the PR8 strain of influenza virus were added to calcium phosphate columns and fractions obtained by elution with phosphate buffers (*p*H 6·8–7·2) of increasing concentrations were tested for infective, haemagglutinating and complement-fixing activity. Elution with 0·2 M phosphate buffer removed most of the protein but little of the haemagglutinin contained in the starting material. By subsequent elution with 0·5 M buffer, 50 to 80% of the original haemagglutinating activity was recovered. The degree of purification estimated on the basis of number of haemagglutinating units per mgm. protein corresponded to 30- to 100-fold of the original material. A 10- to 30-fold concentration of the haemagglutinating activity was obtained by chromatography of the purified material on a second smaller column. Virus infectivity was fully retained after chromatography. The soluble complement-fixing antigen of influenza virus was also purified and concentrated by the method described.

The general application of the method for virus purification was demonstrated by the successful results obtained with Semliki forest virus, vaccinia, encephalomyocarditis, Coxsackie and poliovirus.

H. G. Pereira

ALLEN, R., FINKELSTEIN, R. A. & SULKIN, S. E. **Viral Inhibitors in Normal Animal Sera.** *Texas Reports on Biol. & Med.* 1958, v. 16, No. 4, 391–421. [116 refs.]

This is an extensive review of the literature dealing with viral inhibition by different factors present in normal animal sera. The properties and range of action of heat-stable, heat-labile and lipid inhibitors are presented. The possible role of complement and properdin in the enhancement of virus neutralization by antibody and in the direct inhibition of viral activities is discussed.

[It is impossible to abstract the abundant material included in this review.] *H. G. Pereira*

JADIN, J., GIROUD, P. & VAN WYMEERSCH, H. Néorickettsies isolées à partir d'un cas de leuco-encéphalite sclérosante subaiguë. **[Neorickettsiae Isolated from a Case of Subacute Sclerotic Leuco-encephalitis]** *Ann. Soc. Belge de Méd. Trop.* 1958, Apr. 30, v. 38, No. 2, 189–93, 4 coloured figs. on 2 pls.

An infective agent belonging, according to the authors, to the "neo-rickettsiae" was isolated by mouse inoculation from a case of sub-acute leuco-encephalitis in a European from the Belgian Congo. It was obtained from the blood stream in life and from the brain post-mortem. It was readily seen in smears stained by the Macchiavello method, being about the size of a psittacosis virus. [Insufficient evidence has been produced in this and earlier papers by Giroud and his colleagues that the agents, grouped by them as "neo-rickettsiae", are unrelated either to the rickettsiae of the typhus group or Q fever or to the psittacosis-lymphogranuloma group.] *S. P. Bedson*

VIEUCHANGE, J., DE BRION, G. & GRUEST, J. Virus variolique en cultures de cellules. **[Culture of Variola Virus in Tissue Culture]** *Ann. Inst. Pasteur.* 1958, Dec., v. 95, No. 6, 681–93, 1 text fig. & 6 figs. on 2 pls. [13 refs.]

The authors grew a strain of variola virus in tube cultures of HeLa cells, and bovine kidney and skin cells. Heavy doses of virus (10^6 infectious units) induced rather rapid degenerative changes, with almost complete destruction by the third day. Doses of 10^5 or 10^4 infectious units led to the same sort of changes less rapidly, complete necrosis being evident on the fourth day. Small doses (about 10^3 infectious units) applied to HeLa cells produced focal lesions in numbers proportional to the concentration of virus inoculated. Microscopically, these foci consisted of centres of cellular proliferation. Stained preparations showed vacuolization of cells quite marked at 48 hours with acidophilic or basophilic inclusions within the vacuoles. Proliferative centres were not seen in virus-infected bovine cells, otherwise the cytopathic effects observed were similar to those in HeLa cultures. Culture fluids were titrated at intervals after inoculation with virus: highest titres were attained at 48 hours with large infecting doses, and at 72 hours when less virus was used.

Comparative tests showed that chick-embryo chorio-allantoic membranes and HeLa cell cultures gave much the same result when inoculated with dilutions of a virus suspension, suggesting that these 2 systems are about equally sensitive to the virus. Both antivariolous and antivaccinial sera neutralized the cytopathic effect of variola virus on the tissue cultures. *Colin Kaplan*

HAHON, N. **Cytopathogenicity and Propagation of Variola Virus in Tissue Culture.** *J. Immunology.* 1958, Nov., v. 81, No. 5, 426–32, 6 figs. [31 refs.]

This paper reports experiments with variola virus in cultures of a large number of different mammalian cell lines. The virus multiplied in all of them, though some were better hosts than others. All the cell strains showed rather similar cytopathic changes with the exception of L strain cells which were agglutinated by the virus but not destroyed. A linear relationship was found between log antiserum dilution and log virus neutralized; the author thinks this will make possible a "neutralization test to determine serum antibody titres" [which may be useful for those without the "experience to avoid inherent errors" and variable results with the chorio-allantoic membrane pock inhibition technique which, in competent hands, is reasonably satisfactory].

Colin Kaplan

SHARP, D. G. & OVERMAN, J. R. **Enumeration of Vaccinia Virus Particles in Crude Extracts of Infected Tissues by Electron Microscopy.** *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 409–13, 4 figs.

This paper describes the counting of vaccinia virus particles in unpurified suspensions by the agar sedimentation method. Replicate counts on chick embryo virus and rabbit dermal virus had coefficients of variation of 14% and 10% respectively. The amount of debris in the preparations made it necessary to dilute the suspensions before the virus particles could be clearly seen. Chick embryo virus had to be diluted 1/300 and rabbit dermal virus 1/666. The diagrams showing relationship between relative virus concentration and number of particles per ml. of suspension are strictly linear throughout the dilution ranges investigated. In one experiment with a concentrated and partially purified virus suspension the count was in close agreement with that obtained by the spray droplet method of BACKUS and WILLIAMS. *Colin Kaplan*

WAGNER, S. Immunobiologische Wechselbeziehungen bei der Vaccina- und Herpes simplex Virus-Infektion der Maus. [**Immunological Relations between Vaccinia and Herpes Simplex Virus Infections of Mice**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, No. 5/6, 370–75, 1 fig. [12 refs.]

An investigation of the antigenic relationships of herpes simplex virus and a mouse-adapted strain of vaccinia virus has been carried out by cross-neutralization tests with immune sera prepared in rabbits. Constant volumes of serum were mixed with falling dilutions of the virus preparation and the mixtures were kept at 37°C. for 30 minutes and at 4°C. overnight; each was then inoculated intracerebrally into 3 mice and the sum of the survival times in days was used as a response. This showed a fairly linear relationship against logarithm of virus dose. The dose-response curves for both vaccinia and herpes viruses in the absence of serum were markedly depressed by homologous and heterologous antisera, although the latter had a lesser effect; a considerable degree of cross-neutralization could therefore be demonstrated.

In cross-immunization tests 6 of 29 mice immunized against herpes survived intracerebral challenge with vaccinia virus, and 9 of 25 mice immunized against vaccinia survived intracerebral challenge with herpes virus. *D. J. Bauer*

WHEELER, C. E. **The Effects of Temperature upon the Production of Herpes Simplex Virus in Tissue Culture.** *J. Immunology.* 1958, Aug., v. 81, No. 2, 98–106, 4 figs. on 2 pls. [33 refs.]

3 strains of herpes virus were grown in cultures of HeLa cells and human skin cells at different temperatures, and the extent of development of virus was determined by the inspection of the cytopathogenic effect and by titration in HeLa cell cultures. With incubation at room temperature for 3 days (20·5–27·7°C.) little or no virus was produced; titres from as low as 8 to 44,000 were attained at 30°C., 11,700 to 503,000 at 35°C. and 28 to 42,000 at 40°C. Cultures incubated at 40°C. remained in good condition for 48 hours, when signs of deterioration became apparent. A characteristic cytopathogenic effect was seen in cultures incubated at 30° and 35°; at room temperature the areas of affected cells were very small, and at 40°C. the cells had a shrivelled appearance. Further development of virus occurred when cultures kept at room temperature for 3 days were then incubated at 35°C. for a period. *D. J. Bauer*

WEBSTER, R. G. **The Immunological Relations of the Contagious Pustular Dermatitis Virus to the Mammalian Pox Group.** *Australian J. Exper. Biol. & Med. Sci.* 1958, June, v. 36, Pt. 3, 267–74, 3 figs.

The systematic relationships of the virus of contagious pustular dermatitis (CPD) have been in doubt for some time. This paper not only shows the morphological similarity of CPD virus with the pox viruses, but presents evidence of an immunological relationship. CPD virus from infected sheep was purified by differential centrifugation, and the antigenic relationships of the virus elementary bodies and supernatant fluids was investigated. The supernatant was shown to contain a heat-stable, soluble complement-fixing antigen. This cross-reacted with anti-vaccinial serum, while vaccinia and ectromelia virus antigens fixed complement with anti-CPD serum. There was no cross-reaction with fowl pox. In agar diffusion tests, ectromelia and vaccinia soluble antigens had a minor precipitation against CPD serum in a similar position to the homologous reaction. There was again no cross reaction with fowl pox. In cross-neutralization tests there was no reaction between CPD and vaccinia; however, ectromelia virus was significantly neutralized by CPD serum, although the converse could not be shown probably because the ectromelia antiserum was a weak one.

The author thinks that this is good evidence for including CPD virus in the pox group, and he is probably right. *Colin Kaplan*

DRESCHER, J. Über Hämagglutinin- und Antikörpergehaltsbestimmungen. III. Mitteilung. Über die photometrische Bestimmung von Hämagglutinin und spezifisch hemmenden Antikörpern bei Mumpsvirus. [**The Determination of Haemagglutinins and Antibodies. . . . III. The Photometric Determination of Mumps Haemagglutinin and Inhibiting Antibody**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 1/2, 11–28, 8 figs. [15 refs.]

In previous work [this *Bulletin*, 1958, v. 33, 406 *bis*] the author has described a photometric method for titrating influenza virus and inhibiting antibody, and in the present work the same method has been used with the Enders strain of mumps virus. An example is given of the application of the previously derived formula to the determination of the virus content of an infected allantoic fluid. The theoretical basis of the method depends upon

the size of the red cell agglutinates formed by the virus, and in a comparative study of mumps and the PR8 strain of influenza virus it could be shown from a consideration of the gradients of the extinction curves that the agglutinates formed by mumps virus were smaller, and in a number of replicate experiments it was found that the ratio of the gradients for the 2 viruses was constant. In a somewhat similar manner it could be deduced that fewer particles of mumps virus are needed to form an agglutinate than of influenza. The photometric method was also applied to the determination of the amount of mumps virus remaining after contact with serial dilutions of immune serum, and the reaction between virus and antibody was shown to conform to the Freundlich adsorption isotherm. *D. J. Bauer*

Prieto Lorenzo, A. Nuestra experiencia sobre la inoculación intraocular (cámara anterior) de los virus parotidítico y gripal en el cobaya. [**Inoculation of Mumps and Influenza Viruses into the Anterior Chamber of the Guineapig Eye**] *Med. Trop.* Madrid. 1958, Nov., v. 32, No. 5, 367–88.

Wilcox, W. C., Wood, E. M., Oh, J. O., Everett, N. B. & Evans, C. A. **Morphological and Functional Changes in Corneal Endothelium caused by the Toxic Effects of Influenza and Newcastle Disease Viruses.** *Brit. J. Exper. Path.* 1958, Dec., v. 39. No. 6, 601–9, 12 figs. (11 on 2 pls.) [28 refs.]

Inoculation of influenza A or Newcastle disease virus into the anterior chamber of the rabbit's eye was followed by toxic reactions consisting at first of an apparent fusion of adjacent cells followed by necrosis and complete destruction of the corneal endothelium with consequent corneal oedema and opacity. The lesions were usually reversible and recovered corneas were resistant to challenge with the homologous virus for periods up to 2 weeks after the first inoculation. This resistance could not be related to humoral factors.

The toxic reaction was not associated with detectable virus multiplication. The development of corneal opacity was correlated with alterations in endothelial permeability revealed by an increased accumulation of ^{131}I-labelled albumin in the corneas of the toxic eyes. *H. G. Pereira*

Gostling, J. V. T. **Growth of Influenza 'A' Virus in Cultured Cells of Embryo Mouse Lung.** *Brit. J. Exper. Path.* 1958, Dec., v. 39, No. 6, 679–84. [12 refs.]

The multiplication of influenza virus (A-prime) was studied in cultures of mouse embryo lung. Comparative egg-infectivity titrations of intact and disrupted cell suspensions prepared during the early stages of infection showed that the amount of virus demonstrable in intact cells is up to 10 times higher than that of disrupted cells. These results suggest that the virus fraction rendered "non-infective" during the first 8 hours of infection is responsible for the initiation of virus multiplication. *H. G. Pereira*

Hotchin, J. E., Cohen, Sophia M., Ruska, H. & Ruska, Carla. **Electron Microscopical Aspects of Hemadsorption in Tissue Cultures infected with Influenza Virus.** *Virology.* New York. 1958, Dec., v. 6, No. 3, 689–701, 10 figs. [12 refs.]

Adsorption of erythrocytes to tissue culture cells infected with influenza virus (haemadsorption) was studied by electron microscopy. Adsorption occurred either by direct attachment of erythrocytes to the infected cell membrane, in the absence of visible virus, or by indirect attachment mediated by virus particles or filaments. The terms cyto-haemadsorption and virus-haemadsorption are proposed for the direct and indirect processes respectively. These results suggest that infection by influenza virus causes a change in structure of the host cell wall rendering it capable of adsorbing erythrocytes in a way analogous to the virus haemagglutinin. Implications of these findings on present concepts of structure and mode of formation of influenza virus are discussed. *H. G. Pereira*

Nelson, M. & Lewis, F. A. **A Relationship between Swine and Asian Strains of Influenza A Virus.** *Australian J. Exper. Biol. & Med. Sci.* 1958, Oct., v. 36, Pt. 5, 505–10.

Human sera collected in Melbourne during or immediately after the 1957 Asian influenza epidemic were tested by haemagglutination inhibition and serum-neutralization against the Asian strain and influenza A viruses prevalent before 1935 (Swine) and between 1935 and 1957 (PR8 and FM1). The results suggest that infection with the Asian strain stimulates antibody rises to Asian and Swine strains but not to PR8 or FM1. Tests performed in acute and convalescent sera showed that antibody responses to the Swine strains were of a primary type in children and young adults whereas a secondary type of response was observed in patients more than 35 years old. These findings indicate that a common antigenic component is shared by the Asian and Swine strains.

Age variations of the ratio of clinical to sub-clinical attacks observed during the 1957 influenza epidemic [Keogh *et al.*, this *Bulletin*, 1959, v. 34, 18] are consistent with the finding that the Asian strain appears to be more closely related to viruses prevalent before 1935 than to subsequent strains. *H. G. Pereira*

Takátsy, G. & Barb, K. **New Inhibitor and Erythrocyte Receptor Substances for certain Asian Strains of Influenza Virus.** [Correspondence.] *Nature.* 1959, Jan. 3, v. 183, 52–3. [10 refs.]

The haemagglutination-inhibiting activity of normal sera against an "avid" strain of Asian influenza virus was found to differ in several ways from previously described serum inhibitors. The factor responsible for haemagglutination inhibition of the "avid" strain is heat-resistant and its activity is enhanced by boiling for 30 minutes; it is non-dialysable, and biuret-positive; it is precipitated by 50% acetone, by 66% ethanol and by 0·35 saturated ammonium sulphate. Its action is

abolished by trypsin digestion but scarcely affected by cholera filtrate or potassium periodate.

Red cell receptors for the "avid" strain were not destroyed by treatment with other influenza virus strains (PR8, Lee and a "non-avid" Asian strain) or with cholera-filtrate or periodate. It is suggested that the new inhibitor is a thermo-stable protein or polypeptide. *H. G. Pereira*

GOREV, N. E. **The Use of Broth Culture Filtrates of *Pseudomonas fluorescens* for the Destruction of Non-Specific Thermostable (at 56°C.) Influenza Virus Inhibitors in Human and Animal Sera.** *Acta Virologica.* Prague. 1958, July–Sept., v. 2, No. 3, 171–8. [13 refs.]

Broth culture filtrates of *Pseudomonas fluorescens* were shown to contain a factor destroying normal thermostable serum inhibitors of haemagglutination by influenza virus. This factor differed from the cholera vibrio receptor-destroying enzyme by its lack of action on red cell receptors and on serum inhibitors of haemagglutination by indicator virus strains. The *Ps. fluorescens* inhibitor-destroying factor resisted heating at 56°C. for 1 hour but its activity was greatly reduced at 60°C. and completely abolished at 80°C. Serum treatment by *Ps. fluorescens* filtrates for 1 hour at 56°C. resulted in destruction of normal virus haemagglutination inhibitors and was without effect on specific antibodies. Techniques are described for the preparation and use of *Ps. fluorescens* filtrates in the serological diagnosis of influenza. *H. G. Pereira*

STYK, B., RATHOVÁ, V. & BLASKOVIC, D. **Thermolability of Specific Haemagglutination Inhibiting Antibodies against the FE Influenza Virus and their Reactivation by the Addition of Fresh Serum.** *Acta Virologica.* Prague. 1958, July–Sept., v. 2, No. 3, 179–87.

Part of the specific haemagglutination-inhibiting and virus-neutralizing activities of sera from mice inoculated with an Asian strain of influenza virus was shown to be destroyed by heating at 56°C. for 30 minutes and to be reactivated by the addition of fresh unheated sera. Treatment of fresh sera with zymosan did not abolish this reactivating activity, suggesting that the properdin system is not involved in the reaction. The effect of heat on the specific haemagglutination-inhibiting activity of mouse antisera was less marked with mouse-adapted than with the original virus strain. The inhibitory action of sera from mice inoculated with mouse-adapted strains was more heat resistant than that of sera from mice given the original virus.
H. G. Pereira

MATHEKA, H. D. & ARMBRUSTER, O. **Gradient Elution of Influenza Viruses from Anion Exchange Resin and Demonstration of a Biological Difference between Three Components obtained from the PR8 Strain.** *Virology.* New York. 1958, Dec., v. 6, No. 3, 584–600, 4 figs. [17 refs.]

Physiochemical characteristics of influenza viruses were investigated by ion exchange chromatography with the anion resin Amberlite IRA-400 and elution by a salt concentration gradient technique. Citrate buffer with constant *p*H (6·0) and salt concentration varying between 0·01 N and 1 N was used for elution. Allantoic fluid preparations of influenza strain PR8 were shown to contain 3 physiochemically distinct fractions (designated fractions I, IV and VIII) possessing both haemagglutinating and infective properties. Fraction I was not adsorbed on the resin; fractions IV and VIII were adsorbed at 0·01 N and eluted at about 0·25 N and 0·9 N respectively. Strain FM1 showed 2 fractions (I and II), the first not adsorbed on the resin and the second with maximal elution at about 0·5 N. Strain Lee appeared to contain a single fraction which was not adsorbed on the resin. Small antigenic differences between PR8 fractions I, IV and VIII could be detected by haemagglutination-inhibition but not by neutralization or complement-fixation tests. PR8 preparations obtained by adsorption and elution with fowl erythrocytes were also studied by anion exchange chromatography. Red cell eluates contained 2 fractions (A and B) corresponding to fractions I and IV of the original preparations. Supernatants of red-cell adsorption mixtures showed a new fraction (C) which probably represents an altered form of fraction VIII.
H. G. Pereira

MILLS, R. F. N. **The Effect of infecting the Cells of the De-Embryonated Egg with Influenza Virus on their Uptake of Glucose and Amino Acids.** *J. General Microbiol.* 1958, Dec., v. 19, No. 3, 473–81. [18 refs.]

The uptake of glucose and amino-acids by cells of the chorio-allantoic membrane of de-embryonated eggs was studied and a comparison was made between the behaviour of normal cells and cells infected with influenza B virus. The cells were first starved by maintenance in a simple saline solution. This was followed by inoculation with virus and incubation in the presence of test solutions containing glucose or amino-acid mixtures. Controls were also set up. Virus production and glucose or amino-acid uptake was measured at varying times of incubation. Evidence is presented suggesting that the experimental conditions ensured infection of all the cells exposed to influenza B virus.

Glucose uptake was greater in infected than in uninfected membranes. Uptake of amino-acids from casein hydrolysate or from a defined mixture of 13 amino-acids (EAGLE, *J. Exper. Med.*, 1955, v. 102, 37) was identical in infected and uninfected membranes. When cysteine, histidine or methionine was omitted from the mixture, uptake of the remaining amino-acids was greater in uninfected than in infected membranes, suggesting an increased need of infected cells for these 3 amino-acids. Omission of any one of the other amino-acids from the mixture had no effect on uptake. The possibility of a greater requirement of methionine by infected cells is strengthened by the finding that virus production was inhibited by the methionine analogue ethionine and not by the phenylalanine analogue β-phenylserine. *H. G. Pereira*

GERBER, P. & ADAMS, E. **Development of Resistance of Influenza B Virus to Polysaccharides.** *Science.* 1958, Dec. 19, v. 128, 1571.

An algal polysaccharide extracted from carrageenin (*Gelidium cartilagenium*) protects a proportion of chick embryos against the lethal action of influenza B virus. [Carrageen is an edible seaweed.] A variant strain resisting the action of the polysaccharide emerged after a single passage of the parent virus in treated eggs. The resistant variant was stable on egg passages in the absence of the polysaccharide and did not differ from the parent strain in virulence for chick embryos, multiplication rate in fertile eggs or in serological character. It is suggested that polysaccharide resistance may prove to be a useful marker for studies on virus genetics.

H. G. Pereira

CLARKE, S. K. R. & TYRRELL, D. A. J. **The Neutralization of Influenza and other Viruses by Homologous Immune Serum. Studies in Roller Tube Tissue Cultures.** *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 4, 453–68, 6 figs. [28 refs.]

The neutralization of influenza A virus, poliovirus and adenovirus by specific antisera was studied in roller-tube cultures of trypsinized chick embryo lung, human and monkey kidney, hamster kidney and human liver. Serum neutralization titres obtained against varying virus doses were determined and used for estimations of the slopes of neutralization curves. A slope equal to 1 is obtained when a given increase in virus dose results in a parallel reduction of serum titre. Higher slopes are obtained when large increases of virus dose have small effects on serum titres. Removal of the serum-virus mixtures from the cultures after a period of adsorption caused, in all the systems investigated, a reduction in slope of the neutralization line. It is suggested that the higher slopes obtained when the serum-virus mixtures are not removed are due to the action of antibody on successive cycles of virus production. No evidence of virus neutralization by serum factors other than antibody was obtained. Neutralization titres varied directly with the virus and serum concentration in the reaction mixture. Dilution of serum-virus mixture resulted in virus reactivation.

H. G. Pereira

GENDON, Y. Z. **Study of the Specific Antibody Content of the Individual Protein Fractions of Anti-Influenzal Horse Serum.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 4, 408–14, 4 figs.

The distribution of influenza virus antibodies in protein fractions of horse antisera was investigated by paper electrophoresis and immuno-electrophoresis. Antibodies detected by haemagglutination-inhibition and by virus neutralization were found in the beta, T and gamma globulin fractions, the greater part being present between the T and gamma globulin fractions. Application of these findings to the purification and concentration of influenza virus antibodies is suggested.

H. G. Pereira

VOLUYSKAYA, E. N., TOVARNITSKY, V. I. & BYELIKOVA, A. M. **The Effect of the Properdin System on the Influenza Virus.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 4, 404–7. [12 refs.]

Multiplication of an A-prime strain of influenza virus in the allantoic cavity of fertile eggs was inhibited by normal bovine serum. The inhibitory action of the serum was abolished by adsorption with zymosan and restored by addition of properdin. These results suggest that the properdin system plays an important role in the non-specific neutralization of influenza virus by normal sera.

H. G. Pereira

PEREIRA, H. G. **A Protein Factor responsible for the Early Cytopathic Effect of Adenoviruses.** *Virology.* New York. 1958, Dec., v. 6, No. 3, 601–11, 6 figs. [19 refs.]

The author, with KELLY [this *Bulletin*, 1958, v. 33, 192; *Brit. J. Exper. Path.*, 1957, v. 38, 396], has previously described 2 cytopathic effects of adenoviruses on HeLa cells, an early "toxic" effect and a late effect due to virus multiplication. In this work, using adenovirus type 5, he shows that the early cytopathic effect is due to a protein which is smaller than the virus particle. Thus the supernatant fluid after 3 centrifugations for 1 hour at 150×10^3g showed a 100,000-fold reduction of infectivity (late cytopathic effect associated with intranuclear inclusions and cell destruction) but only about a 3-fold decline in the early cytopathic effect. Crystalline trypsin destroyed the early cytopathic effect without any effect on the final infectivity titre. The factor responsible for the early cytopathic effect is not dialysable. The early cytopathic effect is not really a toxic effect since although the cells are clumped, multiplication is not affected. Also the changes are not progressive and can be reversed by washing the cells. Extracts of normal HeLa cells did not produce any cytopathic effects on HeLa cells. The protein responsible for the early effect was neutralized by type 5 adenovirus immune rabbit serum and by a convalescent serum from a patient infected with type 5 virus.

A. J. Beale

KLÖNE, W. & OELRICHS, Lilly. Untersuchungen zur Cytopathogenität des Adenovirus Typ 3 in Gewebekulturen. [**Investigations on the Cytopathogenicity of Type 3 Adenovirus in Tissue Cultures**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, No. 5/6, 376–89, 12 figs. on 4 pls. [21 refs.]

An account is given of the appearances observed by phase-contrast microscopy in tissue cultures infected with type 3 adenovirus. In monkey kidney cell cultures the nuclei of some cells contained oval or round bodies of varying optical density. There was also loss of definition of the nuclear membrane and disappearance of the nucleoli. The intranuclear bodies enlarged, often becoming angular, and finally occupied the nucleus almost completely. Little change was seen in the cytoplasm. Similar appearances were observed in human amnion cell cultures.

D. J. Bauer

DENNY, F. W., Jr. & GINSBERG, H. S. **Intracellular Localization of Type 4 Adenovirus. I. Cellular Fractionation Studies.** *J. Exper. Med.* 1959, Jan. 1, v. 109, No. 1, 69–83, 1 fig. [23 refs.]

The distribution of virus materials in the cytoplasm and nucleus of HeLa cells infected with adenovirus types 1 and 4 was investigated by a cell fractionation technique involving homogenization in balanced salt solution and separation of cell fractions by differential centrifugation in sucrose solutions. Most of the infective and complement-fixing activities contained in cells infected with adenovirus type 4 were found in association with the cytoplasmic fraction but some activity could also be demonstrated in the nuclear fraction. With adenovirus type 1, on the other hand, a larger part of the infective virus could be associated with the nuclear fraction.

The authors rightly point out that these results are difficult to interpret because of the many sources of error involved in the cell fractionation procedure. It is, however, tentatively concluded that the low activities associated with the nuclear fractions may be due either to incompleteness or to aggregation of the intranuclear virus material. *H. G. Pereira*

BOYER, Georgiana S., DENNY, F. W., Jr. & GINSBERG, H. S. **Intracellular Localization of Type 4 Adenovirus. II. Cytological and Fluorescein-Labelled Antibody Studies.** *J. Exper. Med.* 1959, Jan. 1, v. 109, No. 1, 85–96, 1 text fig. & 16 figs. on 3 pls. [21 refs.]

Morphological changes occurring in HeLa cells infected with adenovirus type 4 were studied by light and phase-contrast microscopy and correlated with production of virus materials detected by the fluorescent antibody technique and by infectivity titrations. The development of nuclear alterations typical of infection by adenovirus type 4 was closely correlated in time with accumulation of intranuclear virus antigen and with production of infective virus. The distribution of virus antigenic material corresponded to that of the granular and crystalline Feulgen-positive structures seen in infected cells. There was no correlation between cytoplasmic fluorescence and production of infective virus. *H. G. Pereira*

PEREIRA, H. G. & VALENTINE, R. C. **Infectivity Titrations and Particle Counts of Adenovirus Type 5.** *J. General Microbiol.* 1958, Aug., v. 19, No. 1, 178–81, 1 pl. [11 refs.]

A purified preparation of adenovirus type 5 was obtained from infected HeLa cells by 3 cycles of homogenization in Arcton 63 with recovery of the aqueous fraction, followed by several cycles of freezing and thawing with centrifuging to remove precipitates. The final preparation was almost water-clear. The virus particles present in it were counted in the electron microscope by the spray method, and the material was also titrated in parallel in HeLa cell cultures, which were observed over a period of 27 days. The number of particles per cc. ranged from $6{\cdot}5 \times 10^{10}$ to $37{\cdot}4 \times 10^{10}$ in 4 preparations, and the number of TCD50 per cc. from $0{\cdot}1 \times 10^{10}$ to $0{\cdot}68 \times 10^{10}$ per cc. Values of 10, 65, 82 and 103 were obtained for the number of particles per TCD50. *D. J. Bauer*

CHANY, C., DANIEL, P., ROBBE-FOSSAT, F., VIALATTE, J., LÉPINE, P. & LELONG, M. Isolement et étude d'un virus syncytial non identifié associé à des affections respiratoires aigues du nourrisson. [**Isolation and Study of an Unidentified Syncytial Virus associated with Acute Respiratory Infections in Infants**] *Ann. Inst. Pasteur.* 1958, Dec., v. 95, No. 6, 721–31, 1 text fig. & 4 figs. on 2 pls. [10 refs.]

A filtrable agent (named EA 102) causing syncytial formations in cultures of KB and HeLa cells was isolated from throat swabs of 2 young children involved in an outbreak of acute febrile respiratory illness. KB cells were more suitable than HeLa cells for isolation and propagation of the agent. Inoculated cultures showed typical lesions consisting almost exclusively of syncytial formations often containing over 100 nuclei. The number of lesions varied directly with the size of virus inoculum. The virus could not be propagated in fertile eggs, was non-pathogenic for newborn mice or for rabbits and did not agglutinate fowl erythrocytes. It was readily inactivated by heat and relatively unstable on storage. During the course of this work an agent identical with EA 102 was isolated from uninoculated cultures of monkey kidney tissue.

The EA 102 agent is not considered by the authors to belong to the myxovirus group, in view of its lack of haemagglutinating activity and its failure to grow in fertile eggs. It is, however, serologically related to the haemadsorption viruses [CHANOCK *et al.*, this *Bulletin*, 1958, v. 33, 621] which have been included among the myxoviruses. The type of lesion caused in tissue cultures distinguishes the EA 102 virus from measles and the chimpanzee coryza agent [MORRIS *et al., ibid.*, 1957, v. 32, 210].

Association of the EA 102 virus with human respiratory disease is suggested by serum-neutralizing antibody rises detected in infants examined during the outbreak under study. The human origin of the virus was also suggested by the presence of EA 102 neutralizing antibody in a high proportion of human sera. *H. G. Pereira*

HALLAUER, C. Züchtung und Abwandlung des atypischen Geflügelpestvirus (NDV) in Explantaten menschlicher Provenienz. [**Cultivation and Variation of Newcastle Disease Virus in Tissue Explantates of Human Origin**] *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 3, 397–409. [19 refs.]

The Valencia strain of Newcastle disease virus was carried through 71 passages in HeLa cells; the virus behaved in a uniform manner throughout, and gave a mean HA titre of 2·1 log units, a mean infectivity titre of 7·5 log units, and an I/H ratio of 5·4. The

cytopathogenic effect took the form of plaque formation progressing to total destruction of the culture. The virus was also carried through 70 passages in human amnion cells and 10 passages in KB and human amnion cells, with essentially similar results. The initial strain killed chick embryos after 40–65 hours, but after 40–70 passages in HeLa cells there was some loss of pathogenicity and the survival time of infected chick embryos was prolonged to 105–144 hours. 75 of 85 (88%) chickens infected with passaged virus by intramuscular injection showed only slight signs of illness and developed inhibiting antibodies in titres of 80 to 1,280. *D. J. Bauer.*

MURPHY, W. H., Jr.; EYLAR, O. R.; SCHMIDT, E. L.; SYVERTON, J. T. **Absorption and Translocation of Mammalian Viruses by Plants. I. Survival of Mouse Encephalomyelitis and Poliomyelitis Viruses in Soil and Plant Root Environment** [MURPHY, EYLAR, SCHMIDT & SYVERTON]. *Virology*. New York. 1958, Dec., v. 6, No. 3, 612–22, 7 figs. [17 refs.] **II. Recovery and Distribution of Viruses in Plants** [MURPHY & SYVERTON]. *Ibid.*, 623–36, 1 fig. [22 refs.]

Extensive investigations of the survival of mouse encephalitis (FA & GD VII) and polioviruses in soil and in plants are reported in detail.

(I) In the first paper it is reported that FA virus survived 3–4 weeks in soil at 30°C. (sterile or unsterile Clarion loam), which is longer than its survival in liquid suspension or sand. GD VII virus survived 5 weeks in soil at *p*H 7·2 and 3–4 weeks at *p*H 8·5, but did not survive 24 hours at *p*H 3·7. Poliovirus was adsorbed to soil—not only Clarion loam but also other loamy or sandy soils and bentonite and kaolin clays. The virus survived for 6–7 weeks in suspension but rather less well in soil especially unsterile soil. The survival of poliovirus around tomato and pea roots was studied. Virus as monkey brain survived longer than as tissue culture fluid. Type 1 virus survived longer in the presence of tomato roots than of pea roots.

(II) The absorption of polioviruses and FA virus by roots of pea, tomato, lettuce and potato plants and the translocation of the virus to the stems and leaves were studied. It was found that FA virus was regularly absorbed by roots but only rarely reached the stems or foliage. Poliovirus except for Type 1 as a mixture of brain and tissue culture suspension was not absorbed by roots. No evidence of virus translocation was found. The poor absorption of poliovirus compared with FA virus is probably due to the adsorption of poliovirus to soil described in the preceding paper.

A. J. Beale

CRAIG, D. E. & FRANCIS, T., Jr. **Contact Transmission of Poliomyelitis Virus among Monkeys.** *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 325–9. [11 refs.]

In each of 4 experiments 5 cynomolgus monkeys were infected with 1×10^7 TCD50 of the Mahoney strain of poliovirus orally and after 8 hours were housed in cages measuring $2 \times 3 \times 3$ ft. with 5 healthy monkeys. 17 out of 20 infected animals were paralysed, and all 20 had evidence of infection (either paralysis or antibody rise and virus excretion). 7 of the animals had a viraemia starting before the onset of paralysis. Excretion of virus was short-lived and irregular but the litter contained virus for the first week of the experiment. Only 8 of the 20 infected animals developed neutralizing antibodies during the experiment (14 days). 2 of the control animals were paralysed and only these 2 developed neutralizing antibodies. 10 of the remaining 18 animals excreted virus for short periods but did not develop an antibody response from which it was concluded that subclinical infection does not occur. Because of this and the short and irregular period of virus excretion it was concluded that orally infected cynomolgus monkeys are not a satisfactory model for epidemiological studies on poliomyelitis

A. J. Beale

MIRONOVA, L. L. **The Characteristics of the MK Strain of Poliomyelitis Virus, Pathogenic for Monkeys, Cotton Rats and Infant Mice.** *Problems of Virology*. London. 1958, v. 3, No. 2, 118–21, 2 figs. [Translated from Russian.]

Russian workers have previously described the isolation of a Type 4 poliovirus. This virus was isolated from patients with paralytic poliomyelitis, caused poliomyelitis in monkeys and was pathogenic for infant mice and cotton rats. Subsequently the virus was found to be serologically identical with Coxsackie A7. Now another virus has been isolated from the pooled faeces of 2 patients with paralytic poliomyelitis by direct inoculations into suckling mice and cotton rats. This virus strain is called MK. It is serologically different from the 3 established poliovirus types, but its relationship to other members of the enterovirus family was not investigated. The MK strain did not produce cytopathic effects in a strain of human fibroblasts. It produced paralysis in monkeys with an incubation period of 2–3 days, but the histological changes were more widespread than those characteristic of poliomyelitis, including involvement of sensory neurones, in the posterior horns and in the post-central convolutions. Lesions were also seen in the leptomeninges. The authors truly observe that more extensive work is required to identify the virus. *A. J. Beale*

HENNEBERG, G. & DRESCHER, J. Beschreibung einer photometrischen Methode zur Virus- und Antikörpergehaltsbestimmung mittels der Erythrozytenaggregation. I. Mitteilung. **[A Photometric Method for the Determination of Virus and Antibody Concentrations by Erythrocyte Aggregation. I.]** *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 1/2, 37–43, 3 figs. (1 coloured on pl.)

The authors have developed a method of haemagglutination titration of non-agglutinating viruses which is based on a new principle. Red cells will agglutinate spontaneously if deprived of their surface negative

charge, but if they are also coated with virus the charge will be partially restored and the size of the aggregates formed by the red cells will bear some relation to the concentration of virus. This working hypothesis was tested with red cells washed with isotonic glucose dissolved in de-ionized water and suspended in the same medium. The suspension was mixed with equal volumes of falling dilutions of the Mahoney strain of poliomyelitis virus inactivated with formaldehyde, and after 80 minutes at room temperature the extinctions of the mixtures were measured in a photo-electric apparatus. In the absence of virus agglutination of the red cells reduced the extinction to a low value, and in the presence of virus a clear relationship could be observed between the virus concentration and the recorded value of the extinction. The appearance of the tubes is illustrated in a coloured plate. It was also possible to employ the method for titration of immune serum.

D. J. Bauer

HARE, J. D. & WARREN, J. **Complement-Fixing Antigens of Live and Inactivated Poliovirus. III. Evaluation of a Sensitive Quantitative Procedure for Complement Fixation.** *Amer. J. Hyg.* 1958, Nov., v. 68, No. 3, 312–21, 5 figs. [13 refs.]

The authors have already described work on the antibody response of guineapigs to living and formaldehyde-inactivated poliovirus using complement fixation to detect antibody [this *Bulletin*, 1958, v. 33, 1093]. In their previous work they used the conventional Kolmer technique for measuring complement fixation. In a search for a more sensitive and quantitative test for measuring poliovirus complement-fixing antigen they have adapted the technique devised by OSLER, MAYER and co-workers [*ibid.*, 1946, v. 21, 775; *ibid.*, 1948, v. 23, 819; *ibid.*, 1952, v. 27, 849]. This method depends upon an accurate spectophotometric method of assaying the haemolysis produced by complement. The amount of complement fixed by an antigen-antibody reaction is measured by titrating the residual complement, and expressing the results in terms of 50% haemolysing doses of complement fixed.

This method proved a reliable technique for the estimation of Type 2 poliovirus complement-fixing antigen in crude tissue culture fluids. If corrections were made for the anticomplementary effects of the tissue culture fluid and antiserum, and spontaneous lysis of the cells, the method was more sensitive and accurate than the Kolmer method. In most experiments a fixation period of 90 minutes at 37°C. was used, but greater fixation was achieved by prolonging the incubation to 120 minutes at 37°C. or 24 hours at 4°C. It was found that inactivation by formaldehyde (1 : 4,000 formaldehyde for 6 days at 37°C.) reduced the poliovirus antigen content 2–3-fold. None of 6 commercially available poliovaccines showed any significant fixation with Type 2 antiserum. A high potency vaccine (vaccine "J") prepared in Dr. Salk's laboratory did show fixation. Only one of the 6 vaccines fixed complement as judged by the Kolmer technique when concentrated 30-fold, but all did when concentrated 100-fold.

A. J. Beale

HUMMELER, K. & HAMPARIAN, V. V. **Studies on the Complement Fixing Antigens of Poliomyelitis. I. Demonstration of Type and Group Specific Antigens in Native and Heated Viral Preparations.** With an addendum by J. H. DINGLE. *J. Immunology.* 1958, Dec., v. 81, No. 6, 499–505, 3 figs. [14 refs.]

There has been considerable difficulty in exploiting the potentialities of the complement-fixation test both for the diagnosis of poliomyelitis and for the study of poliovirus antigens, mainly due to the presence of 2 antigenic components and cross reactions between the 3 serological types of poliovirus. Earlier work has shown that fully infectious virus and inactivated virus react differently in complement-fixation tests and that inactive virus is responsible for most of the cross reactions encountered in the diagnosis of poliomyelitis by complement-fixation. In this paper by adsorbing sera with native infectious virus (N) and heated (H) poliovirus the presence of 2 distinct antigens for each type of virus has been conclusively demonstrated. Moreover, it has been shown that after repeated immunization some sera have antibodies which can be removed equally well by any of the 3 types of heat-treated poliovirus. Adsorption with native (N) antigens reduces the titre of neutralizing antibodies in the same way as those reacting with N antigen in the complement-fixation test. It is not suggested that these 2 antibodies are identical since, for example, neutralizing antibodies appear much earlier in the course of infection than anti N. Whereas Type 1 and 3 N antigens only adsorbed out their homologous antibodies, Type 2 virus adsorbed both Type 1 and 2 anti N from sera. As the authors point out their N and H antigens are most probably identical with the D (N) and C (H) antigens described by MAYER *et al.* [this *Bulletin*, 1958, v. 33, 1094]. They are also the same as the Harvard (H) and Yale (N) antigens described by LE BOUVIER [*ibid.*, 1956, v. 31, 467].

A. J. Beale

PERKINS, F. T. & YETTS, Risha. **Stability of the Potency of Poliomyelitis Vaccine.** *Brit. Med. J.* 1959, Jan. 3, 31–2, 2 figs.

The stability of poliovaccine after storage was investigated by using 3 batches of vaccine stored for 12 months at 4°C. and 1 batch stored for 21 months. In addition 1 batch was also stored at 21°C. and 31°C. for 40 and 100 days. The samples were then stored at 4°C. for 3–5 months and tested for potency with the samples stored all the time at 4°C.

The potency tests were performed in monkeys by the method prescribed for the control of poliovaccine in the U.S.A. It was found that there was no detectable loss of potency in 1 year or in the 1 sample tested 21 months at 4°C. At higher temperatures there was a pronounced loss particularly for the Type 1 component. After 100 days at 31°C. there was little potency of any type remaining.

It is concluded that poliovaccine may be stored for at least 12 months at 4°C. (0–10°C.). Since the Type 1 component lost activity appreciably at 21°C. in 40

days it is recommended that the vaccine should not be left unrefrigerated longer than 7 days. Also it is recommended that the vaccine should not be transported in the tropics without refrigeration, because of the rapid loss of potency at 31°C. *A. J. Beale*

RANZENHOFER, E. R., DIZON, F. C., LIPTON, M. M. & STEIGMAN, A. J. **Clinical Paralytic Poliomyelitis due to Coxsackie Virus Group A, Type 7.** *New England J. of Med.* 1958, July 24, v. 259, No. 4, 182.

The authors report what is apparently the first proved case outside Russia of paralytic disease caused by Coxsackie virus group A, type 7; the patient was a boy of 3 in Louisville, Kentucky, who was admitted to hospital with signs and symptoms characteristic of poliomyelitis. Coxsackie virus A, type 7, was isolated from his faeces, but no poliovirus could be obtained. Neutralizing antibody to Coxsackie A 7 developed during convalescence, the protective titre increasing from 1 : 6 to 1 : 630; no neutralizing antibody to poliovirus was found. *Charles Wilcocks*

KOVAC, W., KRAUS, P. & MORITSCH, H. Wirkung des Elektroschocks auf Virusinfektionen des ZNS der Maus. [**Effects of the Electric shock upon Virus Infections of the CNS of the Mouse**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, No. 5/6, 390–96.

Adult mice were infected intracerebrally with ECHO-9 virus and treated with cortisone and an electric shock of 70 v. alternating current was administered across the temporal regions once daily; after 5–7 days passages were made from the brain and internal organs to further mice. After 5 blind passages no virus could be recovered in tissue culture from the organs. Attempts to adapt a type A Coxsackie virus and the Mahoney strain of Type 1 poliomyelitis virus to adult mice by the same method were also unsuccessful. In similar experiments with a strain of Type 2 poliomyelitis virus pathogenic for mice 4 of 25 treated mice survived, compared with all of 11 controls. *D. J. Bauer*

HSIUNG, G. D. **Some Distinctive Biological Characteristics of ECHO-10 Virus.** *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 387–90, 4 figs.

ECHO 10 virus appears to be odd man out in the enterovirus group of viruses. It is larger in size and has been associated with respiratory illness [this *Bulletin*, 1958, v. 33, 532] and the cytopathic effect is not like that due to polioviruses, the destroyed cells appearing in clumps. It is now reported that ECHO 10 virus is the only human enterovirus which destroys capuchin monkey kidney cells and also those of the swine, cat, dog, guineapig and to a lesser extent calf and rabbit kidney cells. The cytopathic changes are similar to those produced in monkey kidney cells, the virus does not produce plaques under agar. In addition to human enteroviruses, enteric viruses from monkeys (ECMO (HSIUNG, *Ann. N.Y. Acad. Sci.*, 1958, v. 70, 342)) and bovines (ECBO (MOLL and FINLAYSON, *Science*, 1957, v. 126, 401)) were also studied. Only group A ECMO (strains 7853 and SV23) and the ECBO strain shared the wide host range of ECHO 10. It is noted too that these characteristics, wide host range and lack of plaque forming ability, are shared by the adenoviruses. It is concluded that ECHO 10 virus should be removed from the ECHO group.

[According to HOFFERT *et al.*, this *Bulletin*, 1958, v. 33, 1192, the 2 ECHO group A strains studied by Hsuing (7853 and SV23) together with other viruses isolated from monkey faeces and falling into HULL'S group 1 (*ibid.*, 1956, v. 31, 873) produce adenovirus group complement-fixing antigen. It would seem therefore that ECHO 10 is probably an adenovirus.] *A. J. Beale*

LOCKART, R. Z. & GROMAN, N. B. **Some Factors influencing the Interaction of Western Equine Encephalomyelitis and Selected Host Cells.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 163–71, 5 figs.

Western equine virus which had undergone 95 mouse passages was grown in strain L mouse cells and in chick embryo cells. In the absence of cells the virus was found to be rapidly inactivated at 37°C.: in buffered saline its half-life was 17 minutes but this was prolonged to 4 hours or more by the presence of 40% serum or 10% serum + 10% chick embryo extract. There was also considerably prolonged survival in buffered saline which been incubated with cells. When monolayers were infected, washed and overlaid with agar at varying intervals after washing, the plaque count was found to increase with the delay, the limiting factor being the time interval till the release of new virus. The bicarbonate ion appeared to affect adsorption of virus to cell as did an increase in *p*H. Growth curves were determined in the 2 cell types and multiplication was found to be slower in L cells. Virus which had been inactivated by heating at 37°C. was found to cause rounding up of L cells which returned to normal by 3 days later. If cultures were treated with inactive virus 24 hours before infection they produced only 5–37% of the virus produced by untreated cultures. Such auto-interference was also demonstrated in chick embryo cells and the phenomenon is advanced as the explanation of why western equine virus can persist in L cells. The interfering activity of heated virus could be neutralized by specific antiserum and could be removed by centrifugation sufficient to sediment virus particles, thus proving that the property resides in the particles. *C. E. Gordon Smith*

HO, Teh, LIN, Ti-An-Na, LOU, Ai-Lin & CHENG, Yung-Fang. **Protective Action of Repeated Doses of Croton Oil in Japanese B Encephalitis Infection of Mice.** *Chinese Med. J.* Peking. 1958, Nov., v. 77, No. 5, 427–32.

Previous work had shown that a single subcutaneous injection of 5% croton oil in paraffin given to mice

1 day before or on the same day as an infection with Japanese encephalitis significantly reduced mortality. This paper describes the effect of 12 doses given after infections. 50% of mice given 12 doses of 0·5% croton oil (67/133) died compared with 81% (109/135) of controls. 0·05% was almost equally effective but 0·005% had no effect. Daily injections of the broth in which the croton oil had been administered had no effect. The authors believe that the croton oil had some stimulatory protective effect on the central nervous system by causing peripheral irritation.

C. E. Gordon Smith

GRESÍKOVÁ-KOHÚTOVÁ, M. Perzistencia vírusu kliešťovej encefalitídy v mlieku a v mliečnych výrobkoch. [**The Persistence of the Virus of the Tick-Borne Encephalitis in Milk and Milk Products**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 1, 26–32, 5 graphs. [11 refs.]

The English summary appended to the paper is as follows:—

"In their paper, the authors investigated the persistence of the virus of the tick-borne encephalitis in milk and milk products.

"They found that the virus of the tick-borne encephalitis persists very well in cow-milk at the ice-box temperature. Its titre did not fall at all within the interval of two weeks. The authors suppose that milk exercises a protecting influence upon the virus of the tick-borne encephalitis.

"The virus of the tick-borne encephalitis persists very well in cream and butter. The authors found that the titre of the tick-borne encephalitis virus in the butter kept at the ice-box temperature did not fall at all within the interval of two months."

PIERCE, E. C., PIERCE, J. D. & HULL, R. N. **B Virus: its Current Significance. Description and Diagnosis of a Fatal Human Infection.** *Amer. J. Hyg.* 1958, Nov., v. 68, No. 3, 242–50, 2 figs.

Clinical and pathological features of a fatal case of B virus encephalitis are described. The patient was a laboratory technician whose work consisted of caring for normal monkeys and assisting in poliomyelitis vaccine safety tests. No monkey bites were reported by the patient during the 4 months preceding the fatal infection. The disease lasted 3 days and the main symptoms consisted of slight pyrexia, double vision, agitation and delirium. Histopathological examination of the central nervous system revealed intranuclear inclusions typical of B virus in the brain and spinal cord. An agent identified as B virus was isolated by inoculation of brain and spinal suspensions into monkey kidney tissue cultures.

Previous reports of human infections by B virus are reviewed and the importance of the problem in connexion with the manufacture and use of virus vaccines prepared in monkey tissue cultures is discussed.

H. G. Pereira

GAIDAMOVICH, S. I. **The Susceptibility of Domestic Rodents to Neurotropic Viruses.** *Problems of Virology.* London. 1958, v. 3, No. 3, 183–5, 1 fig. [Translated from Russian.]

"(1) On examination of 1272 grey house mice we isolated 48 strains of lymphocytic choriomeningitis virus.

"(2) A characteristic of the isolated strains is their high pathogenicity for white rats and low pathogenicity for guinea-pigs.

"(3) All the strains studied were identical in their antigenic structure.

"(4) We have established a previously unknown high sensitivity of cotton rats to lymphocytic choriomeningitis virus."

IMMUNITY

HOBSON, D., PORTER, K. A. & WHITBY, J. L. **The Immunological Response of Marrow treated X-Irradiated Rabbits to Bovine Gamma-Globulin.** *Brit. J. Exper. Path.* 1959, Feb., v. 40, No. 1, 15–24, 6 figs. [17 refs.]

"Rabbits were exposed to whole body X-irradiation and treated with homologous bone marrow. The donor animals had been previously immunized with bovine γ-globulin. Recipients were challenged with radio-iodinated bovine γ-globulin 1 hr. or 10 days after marrow treatment. At 1 hr. antigen was eliminated in the manner of immune animals. At 10 days no increased rate of removal could be demonstrated. Surviving rabbits were given a second dose of antigen 5 weeks later; those with successful marrow transplants acted as immune animals."

NOSSAL, G. J. V. & LARKIN, Lois. **Failure to induce Immunological Tolerance during Recovery from Irradiation.** [Correspondence.] *Nature.* 1958, Nov. 22, v. 182, 1447–8.

Mice of various ages were irradiated, and some later transfused with bone-marrow cells, in an attempt to induce in them a state of immunological tolerance like that seen in prenatal and neonatal animals. Immunity responses after irradiation were assessed by the ability to form agglutinins after a course of injections of rat erythrocytes. 4 groups of mice were tested: adults exposed to 850 r of X-rays and immediately transfused with marrow from another adult mouse; adults exposed to a sublethal dose of 600 r; adults lethally irradiated and transfused with tissue from 16–17 day-old foetal mice; and 1-day-old mice exposed to 500–700 r. Immunological tolerance was not induced in any of the 4 groups of mice.

I. B. R. Duncan

ASKONAS, Brigitte A. & HUMPHERY, J. H. **Formation of Antibody by Isolated Perfused Lungs of Immunized Rabbits. The Use of [14C] Amino Acids to study the Dynamics of Antibody Secretion.** *Biochem. J.* 1958, Oct., v. 70, No. 2, 212–22, 4 figs. [17 refs.]

By perfusing isolated lungs from hyper-immune rabbits with a balanced salt solution containing amino

acids and 10% normal rabbit serum, the authors demonstrated a considerable net synthesis both of antibody (up to 8 mgm./hour) and of other gamma globulin. The difficulty of differentiation between preformed plasma protein which remains after washing, and proteins newly formed during the experiment, was overcome by injecting into the animal, 1 or 2 days before death, specific antibody labelled with ^{131}I. From the specific activities the proportion of preformed antibodies in the samples could be calculated. ^{14}C-labelled amino acids were added to the perfusion medium and these were incorporated into both specific antibody and other gamma globulin. The rate of synthesis of other gamma globulin was calculated to be rather greater than that of specific antibody. A delay of more than 30 minutes was observed between the addition of labelled amino acids and the appearance of labelled antibody in the medium. The authors offer 2 possible explanations for this delay: antibody may be synthesized from an amino acid pool in equilibrium with the extracellular free amino acids, or from a precursor (protein or bound amino acids). Since intracellular antibody gave a lower radio-activity than would have been expected if intracellular and extracellular antibody had been in equilibrium, it was concluded that the former must have been synthesized in bound form and, therefore, some lungs must contain antibody which is metabolically relatively inert. After 5 hours' perfusion the specific radio-activity of the intracellular free amino acids was only 60% of that of the corresponding amino acids in the perfusion medium at that time, and 6 times that of the amino acids in the intracellular antibody. The authors use these results to discuss a possible mechanism of antibody secretion

R. B. Morrison

WHITE, R. G. **Antibody Production by Single Cells.** [Correspondence.] *Nature.* 1958, Nov. 15, v. 182, 1383–4, 1 fig.

2 methods employing fluorescent antibodies were used in experiments designed to show if a single cell stimulated with 2 antigens will produce antibody to both antigens or only to one. In the first method a frozen section of lymphoid tissue which had previously been treated with antigens A and B was treated with a dilute mixture of A and B and fluorescein-labelled anti-A. After the section had been photographed the fluorescence was abolished by long-wave ultra-violet radiation and the section was treated with fluorescein-labelled anti-B. A second photograph of the original field was taken and comparison of the 2 photographs showed whether fluorescence appeared in the same or in different cells. In the second method a frozen section was treated with a dilute solution of A and B and later with anti-A labelled with fluorescein which gives a green fluorescence and anti-B labelled with rhodamine which gives a red fluorescence.

Sections of spleen from rabbits immunized with pneumococci and with ovalbumin were examined by the first method; sections of popliteal lymph nodes from rabbits immunized into the footpad with diphtheria toxoid and with ovalbumin were examined by both methods.

In all the experiments only one type of antibody was ever detected in any cell. *I. B. R. Duncan*

CLÉMENÇON, G. Azurgranulierte Lymphozyten und ihre Beziehung zur Hepatitis epidemica. [**Experimental Studies on the Relationship of Atypical Lymphocytes to Epidemic Hepatitis**] *Deut. med. Woch.* 1959, Jan. 2, v. 84, No. 1, 38–42, 60, 1 fig. [23 refs.]

The function of azure granules in lymphocytes is unknown and the proportion of lymphocytes bearing granules in normal blood is equally unknown though they appear to be increased in certain infective conditions. The author considered that the increase was related to damage to the liver parenchyma in conditions such as epidemic hepatitis but found that there was no increase in the number of lymphocytes in the circulation bearing azure granules in cases of obstructive jaundice as compared with hepatitis.

The small series of experiments here recorded were devised to determine if the azure granules were an expression of an immunizing or other similar process. Serum was obtained from patients suffering from infective hepatitis, serum hepatitis, infectious mononucleosis and raised blood pressure. The latter 2 served as controls. Leucocytes were obtained by using heparin as an anti-coagulant and removing the leucocyte layer after centrifuging, mixing it with serum and incubating at 37°C. for 30 minutes. Films made and stained with May-Giemsa-Grünwald solution showed an increase in the number of lymphocytes bearing azure granules in leucocytes obtained from patients suffering from epidemic hepatitis as compared with controls. The significance of this finding is discussed and the hypothesis is advanced that the increase *in vitro* of granules in lymphocytes is an expression of an antigen-antibody reaction. *P. A. Clearkin*

DUTTON, R. W., DUTTON, Anne H. & GEORGE, Mariam. **Effect of 8-Azaguanine on Antibody Synthesis** *in vitro.* [Correspondence.] *Nature.* 1958, Nov. 15, v. 182, 1377–8, 1 fig.

In order to test the hypothesis that antibody formation may be mediated by unstable ribonucleic acid templates requiring continual resynthesis, the authors examined the effect of an inhibitor of nucleic acid synthesis, 8-azaguanine, on the production of antibody by suspensions of spleen cells. As a control, the effect of *p*-fluorophenylalanine which inhibits protein synthesis was tested on the same suspensions.

Cell suspensions were prepared from the spleens of rabbits which had been immunized with egg albumin. Leucine labelled with radio-active carbon was added to untreated cell suspensions, suspensions treated with 8-azaguanine, and suspensions treated with *p*-fluorophenylalanine. After 24 hours, antibody to egg albumin which was formed by the cells was recovered by precipitation with egg albumin and added egg albumin antibody, and estimated by the radio-activity of the precipitate. Protein from the spleen cells was isolated and that which had been synthesized during the 24 hours of the experiment was similarly estimated by radio-activity.

Incorporation of radio-active carbon into antibody and into spleen cell protein was inhibited both by 8-azaguanine and by *p*-fluorophenylalanine. It appeared therefore that 8-azaguanine inhibited antibody synthesis in these experiments not specifically by preventing the formation of ribonucleic acid templates but in a general way by depressing protein synthesis, so that this experimental approach did not provide a means of testing the hypothesis of antibody formation by unstable ribonucleic acid templates. *I. B. R. Duncan*

WILSON, M. W. **The Agar Diffusion Precipitin Technique: a Comparison of the Simple and Double Diffusion Methods.** *J. Immunology.* 1958, Oct., v. 81, No. 4, 317–30, 7 figs. [15 refs.]

The relative merits of the double diffusion (DD) and single diffusion (SD) methods of the precipitin test were compared with respect to (1) sensitivity (2) reaction range and reaction time (3) resolving power and (4) artefacts caused by temperature and concentration changes. Specially designed plates allowing parallel observations on SD and DD were employed because the DD method in Oudin tubes may be affected by gravity.

With reactants at equivalent concentrations, DD was found to be more sensitive than SD. With excess antigen the precipitate in DD depends on the length of the column, the diffusion rate and development time—these being unimportant in SD. The time for formation of DD precipitates is directly related to the length of the column and the ratio of the diffusion rates of the reactants; and precipitates will form at any antigen-antibody ratio. In SD the precipitate does not extend far into regions of antibody excess, and formation time is short and hardly varies. The resolving power of DD is slightly better than that of SD, but as individual bands in mixed precipitin systems emerge and disappear at different times, the columns must be observed at regular intervals. Artefacts (gaps and striae) due to sudden changes in temperature or in concentration of reactants are more common in SD than DD.

May F. McCallum

CROWLE, A. J. **Enhancement by Cadmium of Double-Diffusion Precipitin Reactions.** *J. Immunology.* 1958, Sept., v. 81, No. 3, 194–8, 5 figs.

The author describes the enhancing effect of solutions of cadmium salts on the development of precipitin lines in a modification of Ouchterlony's double-diffusion agar precipitin technique. The reaction studied was that between tuberculoprotein and rabbit or guineapig antisera to tubercle bacilli or several of their constituents. It was observed that at equivalent concentrations the sulphate, nitrate and chloride of cadmium were equally active in their enhancement but that whereas all the guineapig antisera were enhanced only some of the rabbit antisera showed any effect. It was found that enhancement by the cadmium ion was given in the range 0·006–0·025%; inhibition was given in the range 0·0002–0·0016%; below 0·0001% there was no action. In addition to increasing the number of lines produced, and their intensity, it was found that the presence of cadmium accelerated the formation of the precipitin lines. With agar dissolved in barbital buffer, cadmium enhanced the activity of both rabbit and guineapig antisera; with agar dissolved in saline, only guineapig antisera were enhanced in their activity; with distilled water neither showed any enhancement. The author found that by varying the antiserum concentration the enhancing effect appeared to affect the antibody and not the antigen; moreover the effect does not appear to be one of partial denaturation of reactant. The author briefly discusses his results in relation to the general importance of heavy metals in biological systems. *R. B. Morrison*

EISLER, M. Über die Wirkung von Adsorbentien auf Antigene und ihre Antikörper. **[The Action of Adsorbent Substances on Antigens and Antibodies]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, June, v. 115, No. 6, 441–8. [17 refs.]

The first part of this paper is a catalogue of the results already described in studies of adsorption of antigens and antibodies by a variety of adsorbing agents: charcoal in various forms, aluminium hydroxide, cholesterin and collodion [see, for example, this *Bulletin*, 1957, v. 32, 1109].

This is followed by a discussion of the general conclusions arising from these results. They are that antibodies are more liable to lose in potency by adsorption than are antigens; but that this loss which is usual in so far as reaction with antigens in solution is concerned is not observed to the same extent in reactions with particulate antigens such as bacteria or red blood corpuscles. There is a contrast here with the effect of precipitins on antibody containing sera. The precipitin is less constant in its action but when it does interfere with antibody its action is more drastic since the antibody is no longer capable of reacting with antigen whether in solution or in the particulate state.

Carbovent, the most active of all the adsorbing agents, tends to destroy both antigen (toxin) and antibody. *J. W. McLeod*

PERKINS, F. T. **A Ready Reckoner for the Calculation of Geometric Mean Antibody Titres.** *J. General Microbiol.* 1958, Dec., v. 19, No. 3, 540–41.

Taking the antibody titres in daily use (from 2 to 4096) the author has tabulated the logarithm of each value and the multiplication of that logarithm by 2, 3, 4, etc. up to 10. Given a frequency distribution of titres (*e.g.* 2 at 8, 3 at 64, 4 at 512 etc.), the required values of the logarithm multiplied by the frequency can be immediately read off and summed (*e.g.* 1·8062 + 5·4186 + 10·8372 etc.).

[This should prove a useful time-saver to workers frequently seeking geometric mean titres.]

A. Bradford Hill

TURK, J. L. **Immune-Adherence with Soluble Antigens.** *Immunology.* Oxford. 1958, Oct., v. 1, No. 4, 305–14, 1 fig. [14 refs.]

Particulate antigens sensitized with antibody and complement adhere to primate red cells, and the phenomenon has been called immune-adherence [this

Bulletin, 1956, v. 31, 685]. It had previously been shown that in certain conditions immune-adherence could be demonstrated macroscopically by the haemagglutination obtained [*ibid.*, 1958, v. 33, 291]. The author has shown that in these conditions, 2 polysaccharide soluble antigens, derived from *Shigella flexneri* and *Salmonella typhi*, and 2 protein soluble antigens, diphtheria toxoid and egg albumin, will cause haemagglutination; this is taken to be evidence of their immune-adherence. A zone of inhibition of haemagglutination (*i.e.* immune-adherence) was observed in the region of antigen excess. Antigen and antibody titrations done by immune-adherence and by complement-fixation were found to be similar.

Streptococcal group A antigen and a batch of purified diphtheria toxoid could not be shown to undergo immune-adherence, although they fixed complement in a complement-fixation test. Residual C'2 (the second component of complement) was detected in immune-adherence tests set up with these 2 antigens, but not with the previously mentioned antigens. Although he is aware of the difficulties of detecting fixation of C'2, the author suggests that these 2 antigens did not undergo immune-adherence because they did not fix C'2. It is known that all 4 components of complement are normally fixed in immune-adherence.

[Bacteria and other particulate antigens, viruses and now soluble antigens have all been shown to undergo immune-adherence which appears to be a general phenomenon involving all systems which fix complement specifically.] *Janice Taverne*

LEVY, A. L. **Complement Levels in Mammals.** *Proc. Soc. Exper. Biol. & Med.* 1958, Dec., v. 99, No. 3, 584–5.

The level of serum complement in human beings and in guineapigs has often been determined but information about its level in other species is limited. The author carried out tests on blood from dogs, Chinese hamster, rat, rabbit and mouse as well as from guineapigs and man by a modification of the method of MAYER *et al.* (*J. Exp. Med.*, 1946, v. 84, 535). He found that the haemolytic complement activity in sera from the rat, dog and hamster was about the same as that in normal human beings, in rabbits it was about one-quarter of the amount and in mice 1/60th. In the guineapig it was 7 times greater than in man.

P. A. Clearkin

CAVALLO, G. & CAVALLO, O. Un nuovo metodo di preparazione del reagente per la titolazione del IV componente del complemento. [**A New Method for Preparing the Reagent for Titrating the 4th Component of Complement**] *Giorn. di Microbiol.* Naples. 1958, Jan.–Feb., v. 5, No. 1, 13–20. English summary (7 lines).

Data are presented to show that complement devoid of the 4th component is prepared more satisfactorily by acidification at low temperature than by the classical method of GORDON and his collaborators (*Biochemical J.*, 1926, v. 20, 1028), *i.e.* treatment with dilute ammonia at 30°C. and subsequent neutralization.

The method recommended is to use 10 ml. of pig's serum cooled to 0°C. to which 2 M acetic acid is added drop by drop until a *p*H of 3·8 is reached, this being controlled by a *p*H meter. The acidified serum is left for 3 hours at 0°C., neutralized with 1 M NaOH and diluted to 30 ml. with veronal buffer.

The serum so treated loses 93% of component IV and only trifling amounts of the other components. Further, the preparation so obtained interferes less with whole complement than does that obtained by alkalinization.

In a detailed table the losses of the different components determined by acid treatment at various *p*H levels at 0°C. and 30°C. are compared with those arising from treatment with alkali. *J. W. McLeod*

CAVALLO, G. L'effetto della diluizione sulla inattivazione termica del complemento. [**The Effect of Dilution on the Thermal Inactivation of Complement**] *Giorn. di Microbiol.* Naples. 1958, Jan.–Feb., v. 5, No. 1, 21–34, 1 fig. [15 refs.] English summary.

The relative rates of inactivation of complement have been studied at 0°C., 30°C. and 37°C. and it has been shown that where an amount of complement producing about 50% haemolysis of the quantity of sensitized blood employed is in play there is considerably greater loss of effect if the complement is diluted before exposure to a temperature of 37°C. than if it is diluted after the period of incubation. This effect is less at 30°C. and practically nil at 0°C. within the periods of exposure investigated—30 to 60 minutes.

It is practically negligible in pig's serum which being less active is used at a lower dilution to give 50% haemolysis of the same amount of sensitized blood

It is also observed that this denaturation at 37°C. is more marked with the first component of complement which is a euglobulin than with whole complement but is not observed to any extent with the other components.

Attention is drawn to the obvious bearing of these observations on the advantage of cold fixation of complement prior to the addition of the haemolytic indicator system and incubation at higher temperatures in reactions for demonstrating the presence of antibodies in sera. *J. W. McLeod*

ZANUSSI, C., TASCHINI, P., INVERNIZZI, F., ORTOLANI, C. & MAZZEI, D. Richerche sul sistema properdinico: su di una eventuale attività antigene dello Zymosan. [**Studies on the Properdin System. Possible Antigenic Activity of Zymosan**] *Giorn. di Malattie Infettive e Parassit.* 1958, Oct., v. 10, No. 10, 931–6. [17 refs.]

The works of PILLEMER and his colleagues [this *Bulletin*, 1955, v. 30, 83] reveal the existence of properdin, a euglobulin of high molecular weight, present in blood serum in small amounts and capable of reacting with a variety of polysaccharides especially that derived from yeast. It is closely linked with the natural bactericidal activity of serum to Gram negative bacteria and from these

observations there have sprung a number of investigations of the influence of Zymosan [the residue from yeast digested with trypsin and extracted with water and alcohol] on the phenomena of immunity. The authors have directed their observations to the phenomenon described by BLATTBERG [this *Bulletin*, 1958, v. 33, 292], *i.e.* the increase in bactericidal power for certain strains of *Escherichia coli* which follows the injection of suspensions of Zymosan to experimental animals.

Groups of rabbits were injected with suspensions of *E. coli* and Zymosan respectively.

Both procedures led to moderate increases in complement, properdin and more marked increases in bactericidal activity for *E. coli* and of agglutinins for suspensions of *E. coli* and Zymosan.

The underlying mechanisms are discussed, especially the possibility that a polysaccharide of close antigenic affinity may be common to Zymosan and some strains of *E. coli*. No firm conclusions are reached and further investigations on these questions are being pursued.

J. W. McLeod

DEWITT, C. W. **Differential Effect of Hog Gastric Mucin on Properdin and Host Resistance to Infection.** *J. Bacteriology*. 1958, Dec., v. 76, No. 6, 631–9, 1 fig. [29 refs.]

"Various samples of commercial hog gastric mucin were examined for their relative ability to promote infection when given intraperitoneally in large amounts simultaneously with the infection, for their *in vitro* and *in vivo* anti-properdin activity, and for the ability of small amounts to produce early nonspecific immunity to a later infection.

"Although there is considerable variation in infection-promoting ability and *in vitro* anti-properdin activity from one mucin sample to another, all samples studied possess a uniformly, high anti-properdin activity *in vivo*. Individual differences in this latter are small and are demonstrable only when low levels of mucin are given. Accompanying this anti-properdin activity are profound changes in the host defenses to infection which do not appear to be causally related to the other factors studied."

Book Reviews

DOUGLAS, J. W. B. & BLOMFIELD, J. M. **Children under Five.** The Results of a National Survey made by a Joint Committee of the Institute of Child Health (University of London), the Society of Medical Officers of Health and the Population Investigation Committee. 177 pp., 8 figs. 1958, London: George Allen & Unwin Ltd., Ruskin House, Museum Street. [21s.]

This is a valuable and unique study of 5,386 legitimate children, from all parts of Great Britain and from all classes, born during the first week of March 1946. The only exclusions are the multiple births. They have been periodically investigated since birth by health visitors, school doctors and school nurses of the local authorities. This volume deals only with the first 5 years. One on the Maternity Services has already been published [this *Bulletin*, 1949, v. 24, 537] and others on the later years are in preparation.

The "losses" have been remarkably few. By 1950 230 (4·3%) had died, of whom 190 were under 12 months of age, and 240 had emigrated. They were mostly non-British families who had been driven here by war. Of the remaining children in the sample only 114 parents refused to supply information and 100 could not be traced but 66 of them were found later. At the examination at 4¼ years only 53% were living at the same address as in 1946.

The principal conclusions are: there was a steady fall in overcrowding during the period, particularly during the first 2 years when war-time housing arrangements were breaking up: the health visitors' reports on the mothers' management and care of their children have been used to pick out the efficient mothers. The proportion of these declined steeply with falling social group, increasing family size and, in the poorer groups, with increasing numbers of small children: children living in county areas were generally taller than those living in towns: maternal care is important, in relation to growth, for the middle range of families where income is sufficient for nutritional needs, if expenditure is carefully planned. For families with larger incomes careful planning is less important and for those with the lowest incomes—perhaps one-quarter of all—no amount of careful planning can compensate for the inadequate income: prematurity explained the greater part of the social group differences found in deaths during the first month of life and pneumonia and gastro-enteritis those between 1 and 12 months: during the first 2 years 37% had at least one infectious disease of childhood and 8% had 2 or more: the poorer children caught these diseases at a younger age: the influence of housing and maternal care on the incidence of childhood infections was negligible and the only thing that made infection more likely was the presence of a school child in the family: there were 1,295 accidents among the survey children during the 5 years: 6 died of accidents and 85 were admitted to hospital: the children who had more than 1 accident were superior in health and physique: the total number of hospital admissions was 1,163: social group differences in tonsillectomy were small.

Public health workers will find part IV of special interest. It deals with the use made of local authority services, the effect on young children of separation from their mothers, "working mothers", bowel training and

bed wetting, prematurity and the effect on child health of home environment.

The children whose mothers made little use of the ante-natal services showed an excess mortality in the first year of life specially in the first month.

52% of the survey children were separated from their mothers at least once during the first 6 years of their lives. If the children remained at home there was no evidence of adverse effect but if they were sent to strange surroundings there was some emotional upset.

4·4% of the 4-year-old survey children were living in homes broken by the death, divorce or separation of their parents. "So far there appear to be no serious disturbances among these children". But this is not final as the present report only takes them up to 5 years.

The proportion of mothers in paid employment increased from 0·8% at 1 month to 4·2% at 1 year and 15·3% at 4 years. 17% of the children aged 2 years of working mothers were in day nurseries or nursery classes. Such children had a higher than normal incidence of the infections of childhood. The report includes a special study of 676 children born prematurely. During the first 2 years they had a high incidence of lower respiratory infections but after 2 they were no more likely to be ill than those of higher birth-weight. Tests of reading and mental ability at 8 years of age showed that an unusual proportion were handicapped in these respects.

There have been previous follow-up reports on substantial groups of children of which the best known is *A Thousand Families in Newcastle-upon-Tyne* [*ibid.*, 1955, v. 30, 190] but the special feature of this survey is that it is nation-wide and not local.

It is an excellent book easily read and well documented. It should find a welcome on the desk of every medical officer of health and superintendent health visitor. *Allen Daley*

SYKES, G. [M.Sc., F.R.I.C.]. **Disinfection and Sterilization.** pp. xviii+396, illustrated. 1958. London: E. & F. N. Spon Ltd., 22, Henrietta Street, W.C.2 [75s.]

In this book the whole field of disinfection and sterilization is covered in under 400 pages. To have done this in so much detail and yet so readably is no small achievement. The approach is historical and scientific in that the development of our knowledge is traced from early beginnings and at all times the author is concerned with the basic principles underlying the methods he describes—yet he succeeds in being up-to-date in referring to the newer methods recently made available, and practical in his description of many applications to medical, pharmaceutical and industrial problems.

The first part deals with the theory of disinfection and methods of testing. After a brief historical introduction and definition of terms the author discusses the chemical, physical and statistical basis of disinfection and then goes on to consider historically and critically the various methods, both official and non-official, for testing disinfectants and antiseptics in use in Britain and the United States of America.

The second part covers methods of sterilization and deals not only with the use of such well established methods as heat and filtration but also with the use of newer methods which are becoming increasingly important such as radiation, gases and vapours (including ethylene oxide) and treatment with cold, desiccation and cellular disintegration.

2 further parts deal with the disinfection and sterilization of air and with the disinfection of viruses, both subjects whose importance is being increasingly recognized and in which much recent progress has been made. There is then a part dealing with chemical disinfectants, including phenols, soaps, alcohols, dyes, quaternary ammonium compounds, halogens and heavy metals.

A final part deals with preservation and the use of preservatives for food, pharmaceutical preparations and various industrial products.

The book is well produced and is exceptionally well documented: there are over 1,000 references indexed both by author and by subject. The text is lucid and readable and there are many tables and illustrations together with a small number of photographic plates.

This book should prove most useful to all who are or may be concerned with disinfection or sterilization, be their interest medical, pharmaceutical or industrial, both as a primary source of theoretical information and practical advice, and as a starting point for more intensive reading. An expert might well find that certain portions of the book dealing with his own particular speciality are not as complete and up-to-date as he would like but this must be true of any work that attempts to cover so wide a field. This book should be the standard British text on the subject for some time to come. *J. C. Kelsey*

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